

REPORT

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Key factors in screening for extended-spectrum beta- lactamase (ESBL)-producing bacteria and carbapenemase-producing organism (CPO)

A narrative synthesis of current evidence

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Sammendrag

Bakgrunn og mål

Betalaktamaser med utvidet spektrum (ESBL) er enzymer produsert av gramnegative bakterier som hemmer virkningen av de vanligste typene betalaktam-antibiotika. Karbapenemase-produserende organismer (CPO) har mekanismer som også gjør dem resistente mot bredspektrede betalaktamer. Det er viktig å forebygge spredningen av disse bakteriene i helseinstitusjoner på bakgrunn av deres resistensmekanismer, høye sykdomsbyrde og begrensede behandlingsmuligheter. Nasjonale anbefalinger for forebygging av spredning av bakteriene i helseinstitusjoner i Norge og Danmark ble oppdatert henholdsvis i 2015 og 2018. I 2023 besluttet Folkehelseinstituttet (FHI) og Statens Serum Institut (SSI) å samarbeide om forslag til oppdaterte nasjonale anbefalinger for screening målrettet mot resistente mikrober og sopp av spesiell betydning for helsetjenesten. Denne litteraturgjennomgangen er en del av en serie gjennomganger som har som mål å frembringe evidens for å støtte prosessen med oppdatering av anbefalingene for screening i helsetjenesten.

Metode

Vi gjennomførte et systematisk litteratursøk i fem databaser etter systematiske gjennomganger, samt primærlitteratur fra de nordiske landene og Nederland. Utfallsmålene i litteraturgjennomgangen var varighet av kolonisering, risiko for smitte mellom mennesker, individuelle faktorer assosiert med ESBL/CPO infeksjon eller kolonisering og prevalens av ESBL-produserende bakterier og CPO i ulike pasientpopulasjoner og settinger. Vi ekskluderte studier om behandling, generell håndtering, laboratoriemetoder, resistens og miljøscreening. Vi valgte å ikke inkludere en diskusjonsdel i denne rapporten, ettersom tolkningen av resultatene vil bli adressert i en mer omfattende rapport som vil samle evidens sammen med andre betraktninger.

Resultater

Vi fant 437 systematiske gjennomganger og 52 primærstudier som var relevante. Studiene viste at kolonisering sannsynligvis avtar over tid, men det er utfordrende å konkludere rundt varighet av kolonisering. Risiko for infeksjon/kolonisering med ESBL-produserende bakterier og CPO etter eksponering er begrenset til noen få settinger. Eksponering kan øke risikoen for overføring, men evidensen er sparsom. Studiene om prevalens i forskjellige settinger viste en relativt høy forekomst av resistens i store deler av verden utenfor Norden, spesielt i Sørøst-Asia og Afrika. Studier på asylsøkere og flyktninger fant bærerskap av multiresistente bakterier på opptil 45 %. Assosierte faktorer med ESBL/CPO-kolonisering var reiser til land utenfor Europa og medisinske reiser. Andre assosierte faktorer var tidligere bruk av antibiotika, kirurgi, respiratorbehandling og kateterbruk.

Konklusjon

Denne litteraturgjennomgangen viste at ESBL/CPO-kolonisering sannsynligvis avtar over tid. Dokumentasjon om smitterisiko er fortsatt ikke entydig. Viktige assosierte faktorer for ESBL/CPO-kolonisering er reise til land utenfor Europa, medisinske reiser, bruk av antibiotika, kirurgi, respiratorbehandling og kateterbruk. Studiene viste også en høy andel bærerskap blant asylsøkere og flyktninger.

Summary

Background and aim

Extended-spectrum beta-lactamases (ESBLs) are enzymes produced by gram-negative bacteria that inhibit the effect of the most common types of betalactam antibiotics. Carbapenemase-producing organisms (CPO) possess mechanisms that also make them resistant to broad-spectrum betalactams. These bacteria are significant in the context of infection prevention and control (IPC) measures in healthcare due to its resistance mechanisms, high disease burden and limited treatment options. National prevention guidelines in Norway and Denmark were updated in 2015 and 2018, respectively. In 2023, the Norwegian Institute of Public Health (NIPH) and the Statens Serum Institut (SSI) decided to collaborate on proposals for new national recommendations for screening targeting resistant microbes of special significance to healthcare. We conducted literature reviews to update screening recommendations for resistant microbes in healthcare. This literature review is part of a series of reviews aimed at providing evidence to support this process.

Methods

We systematically searched five databases for systematic reviews and primary literature from the Nordic countries and the Netherlands. Inclusion criteria included whether outcomes were duration of colonisation, risk of transmission, prevalence of ESBL-producing bacteria and CPO among different patient populations and in different settings, or individual factors associated with ESBL/CPO-colonisation or infection. We excluded studies on treatment, management, laboratory methods, drug resistance, and environmental screening. We did not include a discussion section in this report, as the interpretation of the results will be addressed in a more comprehensive assessment, which will incorporate all evidence syntheses along with other considerations.

Results

We found 437 systematic reviews and 52 primary studies to be relevant. Assessments of duration of colonisation and long-time carriage remain challenging based on identified studies, but there might be a trend that persistent colonisation decreases over time. Evidence on risk of infection/colonisation with ESBL-producing bacteria and CPO after exposure is limited to a few settings in the systematic reviews found. The exposure may increase the risk of transmission, but the evidence is scarce. Studies on prevalence in different setting showed a relatively high prevalence of resistance in countries outside the Nordic region, especially in Southeast Asia and Africa. Studies on asylum seekers and refugees found a colonisation rate of multidrug-resistant bacteria up to 45%. Associated factors with ESBL/CPO colonisation were travel to countries outside Europe and medical travel. Other associated factors were prior antibiotic use, surgery, mechanical ventilation and catheter use.

Conclusion

This overview showed that persistent ESBL/CPO colonization can decrease over time. Documentation on the risk of transmission remains inconclusive. Important associated factors for ESBL/CPO colonization include travel to countries outside of Europe, medical travel, use of antibiotics, surgery, respiratory therapy, and catheter use. The studies also showed a high prevalence of colonization among asylum seekers and refugees.

Background

Extended-spectrum beta-lactamases (ESBLs) are enzymes produced by gram-negative bacteria such as *E. coli* and *Klebsiella* species that inhibit the effect of the most common types of betalactam-antibiotics, including penicillins, cephalosporins, and monobactam. Carbapenemase-producing organism (CPO) possesses mechanisms called carbapenemases that also make them resistant to more broad-spectrum betalactams (1). Two main groups of bacteria are particularly significant in the context of infection prevention and control (IPC) measures in healthcare institutions: 1) Enterobacterales, which are often part of our gastrointestinal flora (particularly Enterobacteriaceae, such as *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*)), and 2) Non-fermenters, which are usually opportunistic bacteria (e.g., *Acinetobacter* spp. and *Pseudomonas* spp.).

Carbapenemase-producing *K. pneumoniae* is increasing significantly in Europe, with great concern. In 2022 the occurrence was reported to be 10.9% in invasive isolates (2). Resistance in *Acinetobacter* spp. showed a decrease in 2022, but in 2021, more than twice as many (+121%) cases were reported to be resistant to each of the three antimicrobial groups (carbapenems, fluoroquinolones, and aminoglycosides) compared to the average for 2018-2019 (3). Carbapenem-resistant *Acinetobacter baumannii*, third-generation cephalosporin-resistant and carbapenem-resistant Enterobacterales and carbapenem-resistant *Pseudomonas aeruginosa* are included in WHO Bacterial Priority pathogens list due to its resistance mechanisms, high disease burden and limited treatment options (4).

In Norway and Denmark, CPO has been mandatory to report (carrier state and infection) since 2012 and 2018 respectively. ESBL_{A/M} is not mandatory to report in either Norway or Denmark. National guidelines to prevent the spread of ESBL-producing bacteria and CPO were last updated in 2015 and 2018 in the two countries respectively and screening recommendations have many similarities. In 2023, the Norwegian Institute of Public Health (NIPH) and Statens Serum Institut (SSI) entered into an agreement to collaborate on proposals for new national recommendations for a screening targeting resistant microbes of special significance to healthcare.

We conducted literature reviews on key research questions for methicillin-resistant *Staphylococcus aureus* (MRSA), resistant enterococci (vancomycin-resistant enterococci (VRE), linezolid-resistant enterococci (LRE) and linezolid-and vancomycin-resistant enterococci (LVRE)), gram-negative bacteria producing extended spectrum beta-lactamase (ESBL), including carbapenemase-producing organism (CPO), and *Candida auris* in order to update outdated recommendations, and investigate opportunities to approach similar recommendations both for the different microbes and in the two countries.

This report is part of a series of narrative syntheses of current evidence for the selected microbes. The working group defined outcomes of interest in advance, which were formulated in a research question. Our aim with the literature review was to find evidence for key factors that are crucial for designing a targeted screening programme, so that we could then use this as part of the decision-making basis for updated screening recommendations in Norway and Denmark.

Methods

Literature search

A comprehensive systematic literature search was conducted on September 22 and 23 2024, in Medline (via Ovid), Embase (via Ovid), Cochrane Database of Systematic Reviews/Cochrane Central Register of Controlled Trials, Web of Science, and Epistemonikos. The searches were performed by a specialist librarian (RAT) at the Library for the Healthcare Administration, Norwegian Institute of Public Health, Oslo, Norway, following an internal peer review by another librarian from the same library. The complete search strategies can be found in Appendices.

Search terms for ESBL/CPO, combined with terms for colonisation including synonyms with appropriate truncations and abbreviations, were used to search titles, abstracts, author keywords, and controlled vocabulary. First, a filter for systematic reviews was added and the results were limited to the years 2014 to the present. To narrow down the search and find relevant primary interventional or observational studies transferable to Danish and Norwegian conditions, a filter for the Netherlands and Nordic countries were applied.

All identified records were added, sorted, screened for duplicates (using different combinations of fields in preferences), and organised in the EndNote 20 software by Clarivate Analytics, Web of Science™.

Research questions

Our research question was:

What is:

- the duration of colonisation of ESBL-producing bacteria and CPO
- the risk of transmission with ESBL-producing bacteria and CPO
- prevalence of ESBL-producing bacteria and CPO among different patient populations and settings
- factors associated with ESBL/CPO infection or colonisation

Table 1. Inclusion criteria

Pico	
Population	Individuals tested/screened for ESBL-producing bacteria and CPO
Outcome	Either of... <ol style="list-style-type: none"> 1. Duration of colonisation with ESBL-producing bacteria and CPO 2. Risk of transmission with ESBL-producing bacteria and CPO 3. Prevalence of ESBL-producing bacteria and CPO among different patient populations and in different settings 4. Factors associated with ESBL-producing bacteria and CPO infection or colonisation
Study design	<ol style="list-style-type: none"> 1. Systematic reviews and scoping reviews (systematic search and inclusion criteria) 2. Interventional or observational studies from the Nordic countries and the Netherlands
Year of publications	2014-present
Country/context	Systematic reviews: No filter Interventional/observational studies: The Nordic countries and the Netherlands
Language	Systematic reviews: English, Norwegian, Swedish, Danish, German Interventional/observational studies: No filter

Exclusion criteria:

- Studies on treatment outcomes
- Studies on management of cases with ESBL-producing bacteria and CPO
- Studies on laboratory methods (including sampling methods) for detection of ESBL-producing bacteria and CPO Studies investigating levels of drug resistance
- Studies concerning genetically related resistant gram-negatives or cell biology
- Studies exclusively concerning environmental screening, nor studies regarding sampling in the environment during outbreaks
- Studies on preventive measures (including screening) against postoperative wound infections
- Narrative reviews, primary studies, letter to the editor, abstracts/posters, non-peer-reviewed studies, correspondence, short communications, comments
- Letter to the editor, abstracts/posters, non-peer-reviewed studies/reports, correspondence, short communications, comments
- Outcomes not reported for ESBL-producing bacteria and CPO specifically

Study selection

We used EPPI-reviewer as a screening tool (5). One researcher (LEØ) screened all the articles using their titles and abstracts. It was planned double screening of titles and abstracts, and that disagreements or uncertainties should be addressed through discussion with another researcher acting as an arbiter (MM), but due to resource challenges this was not adhered to. However, overall inclusion/exclusion criteria were discussed in connection to the literature review of *C. auris* mentioned in the introduction. Outcomes of these discussions were also relevant for this review, although it did not address studies on ESBL-producing bacteria and CPO specifically. LEØ reviewed the full texts of included articles and made the final selection decisions. Remaining uncertainties regarding full text inclusion were resolved through discussion between the researchers (LEØ and MM). An expert on review methodology (JH) provided feedback on the study selection process and methodological approach of the literature reviews performed.

In this report, we use *outcome of interest* to refer to the key factors we looked for in the studies, and which are operationalised in our research question. Namely, the duration of colonisation, risk of transmission, prevalence among different patient populations and in different settings, and individual factors associated with colonization or infection of ESBL-producing bacteria and CPO. For studies from the Nordic countries and the Netherlands, we looked only at the outcome; duration of colonisation, associated factors and prevalence among different patient populations and in different settings.

In this report, we do not distinguish between intermittent and persistent carriers of ESBL-producing bacteria and CPO, and we consistently use colonisation to describe carriage in these groups.

Data extraction

Four researchers (ASD, LEØ, HMEV, MM) extracted data points concerning the outcomes of interest. For all included studies, we extracted information on author, year, the country of study, study objective and authors conclusion.

For the systematic reviews we extracted information on search period, databases, setting/population, pathogens, number and type of studies included and number of patients. We believe this data is important for assessing confidence in the results and transferability to a Nordic setting.

For the primary literature from the Nordic countries and the Netherlands, we extracted data on study period, study design, setting/population and number of patients included for all studies. In addition, we added variables relevant for the outcome of interest and for the strength of the results and their importance for new screening recommendations.

Data analysis

For each outcome of interest, we created tables summarising the relevant studies. Each table lists the studies reporting on the specific outcomes, along with the variables relevant for the outcome.

A narrative synthesis of the literature on each of our four outcome categories were then made.

Chosen limitation in the structure of this report

We chose not to include a discussion section in this report, as the interpretation of the results will be addressed in a more comprehensive assessment, which will incorporate all evidence syntheses along with other considerations such as ethics and economics.

Results

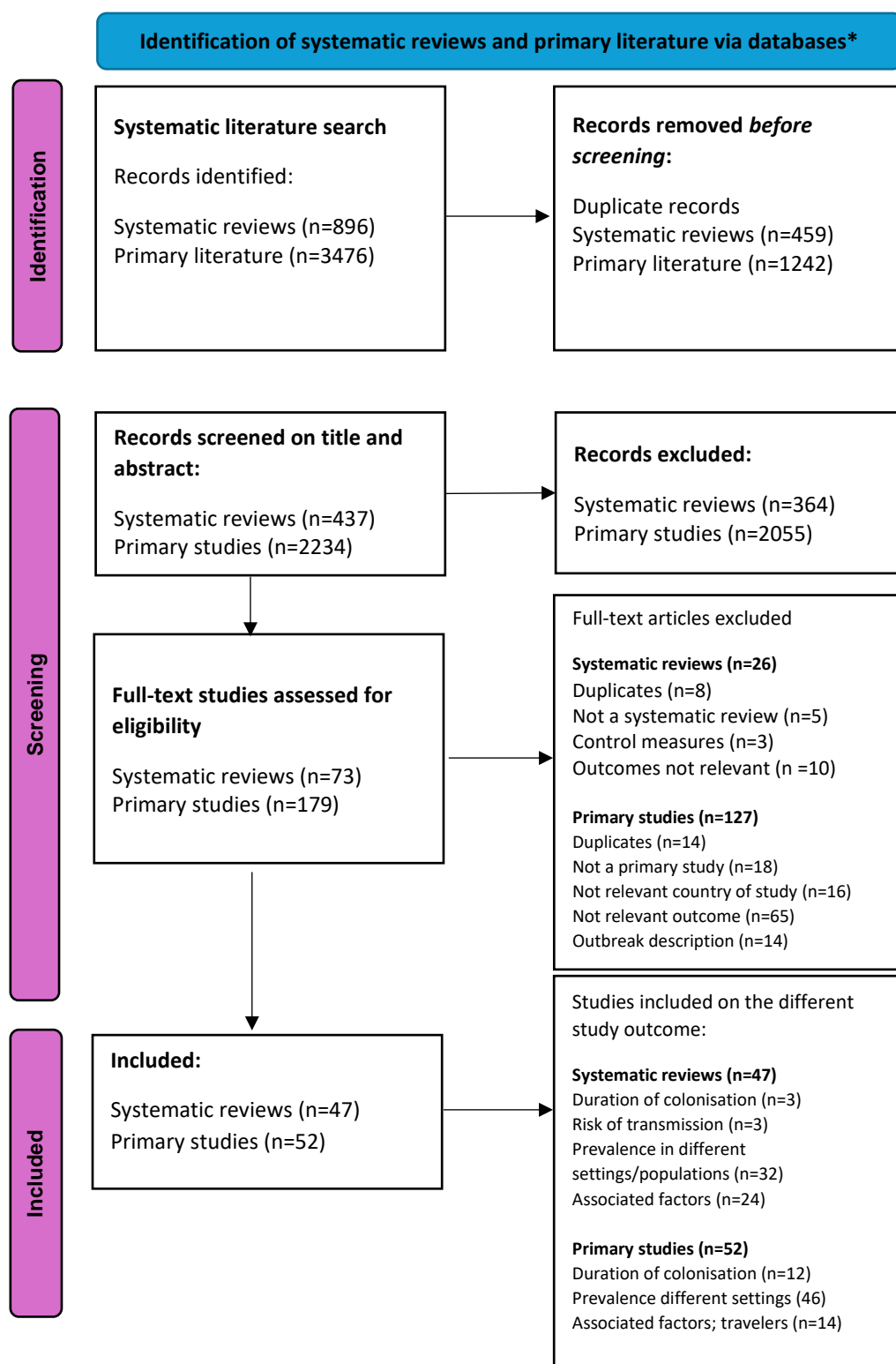
Selected studies

Systematic reviews

After removal of duplicates, we identified 437 systematic reviews (Figure 1). Upon screening titles and abstracts, we selected 73 studies for full-text screening. On full-text screening, 26 of these studies were excluded for not meeting the inclusion criteria. A total of 47 full-text articles were included in the review. Publication dates ranged from 2015 to 2024. Selected studies addressing our outcomes of interest was duration of colonisation (n=3), risk of transmission (n=3), prevalence in different populations/settings (n=32), and associated factors (n=24).

Primary studies from the Nordic countries and the Netherlands

Through the literature search on studies from the Nordic countries (Denmark, Finland, Iceland, Sweden and Norway) and the Netherlands, we identified 2234 primary studies (Figure 1). After screening titles and abstracts 179 references met the inclusion criteria. On full-text screening, 52 articles were considered relevant and included, reporting on the duration of colonisation (n=12), on associated factors; travellers (n=14) and on prevalence in different populations/settings (n=46).



* Ovid Medline(R) and Epub Ahead of Print, Embase, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Web of Science and Epistemonikos.

Figure 1. Flow diagram of search strategy and study inclusion.

Narrative synthesis

1. Duration of colonisation with ESBL-producing bacteria or CPO

Systematic reviews

Three systematic reviews were found reporting on duration of colonisation (6-8). The reviews included studies from different countries, mostly European countries, but also from USA, Asia, Oceania and South America. Number of included studies varied from 11 to 37. The population were mainly adult persons; travellers, community residents, healthcare workers/students and patients in hospitals and long-term care facilities. The studies are summarized in Table 2.

Bar-Yoseph et al. (6) studied the duration of ESBL-producing Enterobacteriaceae and carbapenem-resistant Enterobacteriaceae (CRE) colonisation in hospital patients and community residents. They found that colonisation decreased from nearly 77% at one month to 35 % at 12 months in patients in healthcare settings. Carriers in the community had a lower risk of colonisation rate with 52 % remaining colonised at one month and 19.2% at 6 months.

Hassing et al. (7) studied the duration of multidrug-resistant Enterobacteriaceae (MRE) colonisation among travellers recruited from travel clinics and found that colonisation rate after 6 months was 6-24% in five studies. One study screened cases at 1,2,3,6 and 12 months and found a colonisation rate of 34%, 19%, 10%, 5% and 2% respectively. Travellers to Asia showed longer duration of colonisation compared to travellers to other countries. Colonisation of multidrug-resistant *E. coli* had a lower risk for prolonged colonisation than other multidrug-resistant species.

Ling et al. (8) studied the duration of ESBL producing Enterobacterales (ESBL-E) colonisation in the community and found that half of the carriers lost ESBL-E colonisation after two months. Twenty-four percent (95% CI: 15–34) remained carrier at 6 months and seventeen percent (95% CI: 5–30) and thirteen percent (95% CI: 12–38) remained persistent carriers 24 and 36 months from baseline, respectively. They found that travellers had shorter duration of colonisation (median 1-2 months) compared to discharged hospital patients (median 6 months).

Primary studies from the Nordic countries and the Netherlands

We included 12 primary studies from the Nordic countries and the Netherlands that investigated the duration of colonisation. Eight of the studies (9-16) were already included in one of the systematic reviews (8) and will not be mentioned further. The remaining four studies (17-20) will be summarised in Table 3.

van der Putten Boas et al. (17) studied the duration of ESBL-producing *E. coli* (ESBL-Ec) colonisation in healthy travellers and compared 34 long-term carriers (≥ 12 months) with short-term carriers (< 1 month). For each long-term carrier, two short-term carriers were matched by age, sex and travel destination. Long-term colonisation was found to be driven by a special lineage of ESBL-Ec.

The 17 travellers that carried the same ESBL-Ec strain carried it for at least a year after return from travel. The population used in this study is the same population used in Arcilla et al. (9) included in Ling et al. (8).

Van Duijkeren et al. (18) followed a group of patients with positive and negative ESBL-producing *E. coli* and *K. pneumoniae* (ESBL E/K) over time in the community. The patients were asked to take five faecal samples (T1-T5). The colonisation rate was 51.3% at sample T1 (median four months since the initial sample), 49.3% at T2 (median, five months), 44.0% at T3 (median, six months), 43.1% at T4 (median, 7.1 months), and 42.7% at T5 (median, 8.0 months). Of the 76 positive participants 25 (32.9%) tested positive for ESBL E/K in all the samples covering a period of 242 days (> 8 months).

Van Weerlee et al. (19) studied duration of multidrug resistant Enterobacterales colonisation among discharged patients from hospital and community residents visiting their general practitioner (GP). They followed the participants for 12 months and found that 16.7% were intermittent carriers and 40.3% were persistent carriers. There was no difference in clearance between the discharged patients and GP patients.

Weterings et al. (20) studied duration of ESBL-producing *E. coli* (ESBL-EC) in nursing home residents. They compared duration of colonisation of ESBL ST131 and non-ST131 and found a median time for clearance of 13 and 11.2 months respectively. The median time to clearance in the ESBL-ST131 group was significantly longer in residents who were ESBL-ST131 colonised upon entering the study than in residents who acquired ESBL-ST131 during the study.

Table 2. Overview of characteristics and findings from systematic reviews on the duration of ESBL/CPO-colonisation

Author (Year)	Country	Search period	Databases	Setting/ population	Pathogens	Study objective	No. studies incl.	Type of studies incl.	No. of patients	Comments	Authors' conclusion
Bar-Yoseph (2016)	Europe, China, Australia, USA, Asia	Up to november 2015	PubMed, Cochrane, EMBASE, Google Scholar	Mainly adults. Hospital- and LTCF patients, community residents	ESBL- E and CRE	Estimate CRE and ESBL colonisation duration and evaluate the effect of decolonisation therapy	37	Cohort studies, case-control studies, RCT, case series	2614	Colonisation was assessed at 1, 3, 6 and 12 months. Clearance was defined by 3 negative rectal swabs, but based on a single negative rectal swab in 18 studies and on ≥2 in 16 studies	Colonisation rates without intervention decreased from 76.7% at 1 month to 35.2% at 12 months in healthcare-settings. In the community; 52.3% remaining colonised at 1 month and 19.2% at 6 months
Hassing (2015)	Northern and Western Europe, Australia, USA	Up to august 2015	PubMed, EMBASE, Scopus, MEDLINE, Web of science, Cochrane, google scholar	Healthy adults traveling. Median age 25-66 years. Travellers visiting a travel clinic, hospital staff, healthcare students	MRE	Identify travellers' risk of acquisition of colonisation of MRE, duration of MRE-colonisation and MRE transmission to household contacts	11	Cohort studies	2331	The mean duration of travel was 14–21 days	Colonisation rate after 6 months was 6–24% in five studies. One study tested cases 1,2, 3, 6 and 12 months and found a colonisation rate of 34%, 19%, 10%, 5% and 2% respectively. Travellers to Asia showed longer colonisation compared with other destinations. colonisation of MDR E. coli had lower risk for prolonged colonisation than other MDR spp.
Ling (2022)	Europe, USA, New Zealand, Asia, South America	Up to april 2021	PubMed, EMBASE, Scopus	Mainly adults. Community residents, discharged hospital patients, travellers	ESBL-E	Estimate the duration of ESBL-E colonisation in the community and household transmission rates	26	Cross-sectional, cohort studies	2505	14 studies investigated the duration of colonisation in discharged hospital patients, 10 studies in international travellers (mainly Asian countries) and 2 studies in the general community. The follow-up period of the studies ranged from 1 to 36 months. Most studies assumed eradication in participant after one negative culture	The median colonisation duration was 2 months. 24% remained carriers at 6 months, and approximately 17% and 13% persisted after 24 months and 36 months. Travellers had significantly shorter colonisation (median 1–2 months) than discharged hospital patients (median 6 months) at all measured time points

ESBL-E; Enterobacterales/ Enterobacteriaceae producing extended-spectrum beta-lactamase, MRE; Multidrug-resistant Enterobacteriaceae (ESBL-E, pAmp C-E and CPE – carbapenemase-producing Enterobacteriaceae), MDR; multi-drug resistant, CRE; carbapenem-resistant Enterobacteriaceae, LTCF; long-term care facility, RCT; Randomized controlled trial.

Table 3. Overview of characteristics and findings from primary studies from the Nordic countries and the Netherlands on the duration of ESBL/CPO colonisation

Author (Year)	Country	Study period	Study design	Setting/ population	Pathogens	Study objective	Comment	No. Of patients	Positive patients	Loss to follow-up	Follow-up time	Screening interval	Clearance defined	Authors' conclusion
Van der Putten Boas (2024)	The Netherlands	2012 – 2013	Cohort study	Travellers. Adults Median age 50.5 years (IQR 32.8–60.7)	ESBL	Identify which ESBL-Ec lineages are associated with increased colonisation duration after travel	The main purpose for travel was tourism, median travel duration was 20 days	2001	633	49	12 months	1,3,6,12 months	Not specified	17 travellers carried the same ESBL-Ec strain for at least a year after return. Long-term colonisation was mainly driven by a special lineage for ESBL-Ec. Antibiotic usage was low before, during and after travel and was similar between the two groups. None of the travellers hospitalised
Van Duijkeren (2018)	The Netherlands		Cohort study	Community residents. Adults (20->60 years)	ESBL	Investigate duration of and risk factors for prolonged colonisation of ESBL	Some participants in a cross-sectional study participated in longitudinal study	325	107. Long-term colonisation 25	-	>8 months	Monthly. Median study duration was 243 days	Not specified	ESBL-E/K colonisation persisted for >8 months in 32.9% of the initially positive individuals, while 12.4% of initially negative acquired ESBL-E/K. Risk factors for prolonged colonisation: antibiotic use (previous 6 months), proton pump inhibitors, living near pig farm and travel to Africa/Asia/Latin America
Van Weerlee (2020)	The Netherlands	2013 – 2016	Cohort study	Hospital patients, Community residents. Adults (median age 69)	ESBL	Assess duration of colonisation of MDR Enterobacteriales among discharged hospital patients and patients attending their GP	>40% were included from the hospital setting, most had underlying morbidity (86.1%)	101	101	76	12 months	3,6,12 months	One or more negative cultures without a subsequent positive culture at 12 months	16,6% were classified as intermittent and 40.3% as persistent carriers. Of the intermittent carriers, the majority had two negative cultures during the study period. There was no difference in clearance between discharged hospitalized and GP patients. The only factor associated with clearance at 12 months was not traveling to a foreign country (OR=3.5)
Weterings (2022)	The Netherlands	2013 – 2019	Several PPS	Nursing home. Adults (median age 82 years)	ESBL	Assess the duration of rectal ESBL-producing E. coli (ESBL-EC) colonisation in residents in a nursing home	23-point prevalence surveys were performed at intervals of three to six months	1806	116	4	Median follow-up time 17,9 months	23 PPS were performed at intervals of 3-6 months	≥ 1 negative swab/when strain typing showed a different MLST or cluster type	Median time to clearance was 13 months for ESBL-ST131 compared to 11.2 months for ESBL-non-ST131. Residents who were ESBL-EC positive in their first survey, the median time to clearance for ST131 was 59.7 months compared to 16.2 months for ESBL-non-ST131. Residents who acquired ESBL-EC, the median time to clearance for ST131 was 7.2 months compared to 7.9 months for ESBL-non-ST131

ESBL eC/EC – Extended spectrum beta-lactamase E. coli, MDR; multidrug resistant, GP; general practitioner

2. Risk of transmission

Systematic reviews

Three systematic review was found reporting on risk of transmission of multidrug-resistant (MDR) gram-negative bacteria (GNB) (7, 8, 21). The studies are summarised in Table 4.

Hassing et al. (7) and Ling et al. (8) studied transmission in households. Hassing et al. included one study that screened household contacts for Multidrug-resistant Enterobacteriaceae (MRE) after return of the index traveller. Two of eleven contacts were found MRE-positive, but both carried a different ESBL-producing *E. coli* based on multilocus sequence typing (MLST) than the associated traveller.

Ling et al. included 11 studies (cross-sectional and longitudinal studies) reporting on household transmission. They found that 18.4% to 35.2% of contacts became carriers within 4 to 36 months range of follow-up time from discharge of index hospital patient. ESBL-E transmission from return travellers to household contacts was lower, with only 18.2% and 7.7% of contacts acquiring colonisation after 6 and 12 months, respectively, from traveller's return.

Bulabula et al. (21) studied transmission from colonised mothers to their infants and included eight studies from different countries in Europe, Middle East, Asia, and Africa. They found that the pooled proportion of GNB MDR transmission from colonised mothers to infants was 27% (95% CI: 8-47%). For ESBL-producing Enterobacteriaceae, the transmission rate was 32% (95% CI: 1-62%).

Primary studies from the Nordic countries and the Netherlands

In this narrative synthesis we didn't look at primary studies for the outcome risk of transmission.

Table 4. Overview of characteristics and findings of systematic and scoping reviews on risk of transmission of ESBL/CPO.

Author (Year)	Country	Search period	Databases	Setting/ population	Pathogens	Study objective	No. studies incl.	Type of studies incl.	No. of patients	Comments	Authors' conclusion
Bulabula (2020)	Europe, Middle East, Asia, Africa	Up to march 2019	PubMed, Scopus	Mothers and their infants	MDR Gram-negative bacteria, including ESBL-producing Enterobacteriaceae	Investigate transmission of MDR-GNB from colonised mothers to their infants	8	Cohort studies, cross-sectional studies	147 mother-infant pairs		The pooled proportion of MDR-GNB transmission from colonised mothers to infants was 27% (95% CI: 8-47%). For ESBL-producing Enterobacteriaceae, the transmission rate was 32% (95% CI: 1-62%)
Ling (2022)	Europe, USA, New Zealand, Asia, South America	Up to april 2021	PubMed, EMBASE, Scopus	Mainly adults, but also children. Community residents, discharged hospital patients, travellers	ESBL-producing Enterobacterales	Estimate the duration of ESBL-E colonisation in the community and household transmission rates	26	Cross-sectional, cohort studies	2505	There were insufficient data to robustly meta-analyze household transmission	Five longitudinal studies reported 18.4% to 35.2% of contacts acquired ESBL-E within 4 to 36 months from hospital discharge of index case. Transmission events from travellers to their contacts appeared lower. Travelers with travel-acquired ESBL-E had significantly faster decolonisation rate than discharged patients, suggesting that travel-associated import of MDR pathogen may have limited contribution to community transmission of ESBL-E
Hassing (2015)	Northern and Western Europe, Australia and USA	Up to august 2015	PubMed, EMBASE, Scopus, MEDLINE, Web of science, Cochrane, google scholar	Healthy adults traveling. Median age 25-66 years. Travellers visiting a travel clinic, hospital staff, healthcare students	MRE	Determine the effect of international travel on the risk of acquisition of faecal colonisation of MRE	11	Cohort studies	2331	Household contacts were defined as persons who shared the same household with a participant on a regular basis	One study (370 participants) screened household contacts for MRE after return of the index traveller. Two of 11 contacts were found MRE-positive. Both carried a different ESBL-producing E. coli based on multilocus sequence typing (MLST) than the associated traveller

ESBL-E: Enterobacterales producing extended-spectrum beta-lactamase, MDR – Multi-drug resistant, MRE - Multidrug-resistant Enterobacteriaceae.

3. Prevalence of colonisation in different patient populations and settings

Systematic reviews

We found 32 systematic reviews (7, 22-52) that reported on the prevalence of ESBL/CPO-colonisation in different populations and settings. The studies are summarised in Table 5. The systematic reviews were published between 2015 and 2024 and covered studies from all continents. The reviews showed variation in included populations and settings like patients in hospital, long-term care facility or conflict zones and travellers, healthcare workers and individuals in the community.

The reviews showed a relatively high prevalence of resistance among hospitalised patients in general (22,24,25,49,50) and in specific groups within healthcare (23,28,30,31,37,39,41,42,44,46,48) in large parts of the world outside the Nordic region. The highest rates were found in Southeast Asia and Africa (23-25,27,37,41,42,44), but also within Europe, where high prevalences were seen in Southern and Eastern Europe (23,24,32). In a systematic review by Peters et al. (47) an ESBL prevalence among healthcare workers between 2.6% and 48.5% was shown in a total of 13 studies from Europe, Asia, Africa and North and South America. Flokas et al. (32) looked at colonisation rate of ESBL-producing bacteria among long-term care facility residents and found a pooled prevalence of 18%. Colonisation rates were 31% in Asia, 18% in Europe, 13% in North America and 8% in Oceania.

One review identified a high prevalence of resistant gram-positive and gram-negative bacteria among pilgrims to Mekka (40) and studies among healthy individuals in the community also found a high prevalence of resistance (26,27,38), with the highest rates in Southeast Asia (27,38). Granata et al. (35) studied prevalence of antibiotic resistance in conflict settings and found a prevalence rates

(>60%) of ESBL-producing *K. pneumoniae* and *E. coli* in Iraq and Afghanistan. Prevalence of CPOs were reported in Ukraine and Libya, with resistance rates of 80% for some carbapenemases. Fulchini et al. (33) found ESBL-prevalence among refugees from 9-24%.

Studies on travellers (7,29,33,34,36,45,51,52) are described in more detail in the section on associated factors.

Primary studies from the Nordic countries and the Netherlands

We found 46 studies (9,10,14,16-20,53-55,56,68-72,73-101) that looked at prevalence in different populations like travellers and asylum seekers/refugees and in different settings like nursing homes, hospitals and daycare centers. Here we chose to only focus on the studies on prevalence among asylum seekers/refugees and patients hospitalised abroad and the studies are summarised in Table 6. Prevalences in other settings are described thoroughly in the systematic reviews. Primary studies on travellers are described in more detail in the section on associated factors.

Studies on asylum seekers and refugees (53-56) found colonisation of multidrug-resistant bacteria in 20-45% and that ESBL colonisation was most common. Studies included on prevalence in patients hospitalised abroad found that colonisation by MDR bacteria was common. ICU treatment, short time since hospitalisation and antibiotic use were identified as predisposing factors. Colonisation rates were highest for transfers from Asia (71.9%) and lowest for those within Europe (12.5-18.9%). ESBL colonisation was more common than other MDRO (71,75). Similar findings are described in Khawaja et al. (76). Westerholt et al. (77) also found a higher rate in patients transferred from southern and Western Asia and found a detection rate for CPO of 1.5%.

Table 5. Overview of characteristics and findings of systematic reviews on prevalence of ESBL/CPO in different populations and settings.

Author (Year)	Country	Search period	Databases	Setting/ population	Pathogens	Study objective	No. studies incl.	Type of studies incl.	No. of patients	Authors' conclusion
Abera (2023)	Several	2016 – 2022	PubMed, Google Scholar, Web of Science	Hospitalised patients	ESBL-E/CPE	Assess colonisation rate and risk factors of ESBL-PE and CRE colonisation among hospitalized patients at the global level.	20	Cross sectional, case-control and cohort	ESBL: 11647 CRE: 8733	Pooled estimate of ESBL-E colonisation was 45.6% The predominant ESBL producer was E. coli, 32.99% followed by K. pneumoniae, 11%. The pooled estimate of CRE colonisation was 16.19% (most common K. Pneumoniae)
Alevizakos (2016)	Several	Up to april 2016	PubMed EMBASE	Hospitalised patients	ESBL-E	Estimate prevalence of gastrointestinal colonisation with ESBL-PE cancer populations and determine the risk for subsequent bloodstream infection (BSI) with these pathogens.	10	Cohort studies	2211	The pooled prevalence of ESBL-E colonisation was 19%. Stratifying per region, the pooled prevalence in Europe was 15% whereas in Asia the pooled prevalence was 31%. In addition, the pooled prevalence was 15% among patients with haematological malignancy. Patients with malignancy who were colonised with ESBL-PE had an almost 13 times higher risk of developing BSI with ESBL-E during their hospitalisation.
Alevizakos (2017)	France, Ireland, USA	Up to april 2016	PubMed EMBASE	Organ transplanted adults, some pediatric	ESBL-E	Identify prevalence of ESBL-PE colonisation of the GIT among patients with malignancies	4	Cohort studies	1089	Among SOT patients, approximately one in five patients is colonized with ESBL-E. The pooled prevalence of ESBL-E GI colonisation in the studied population was 18% (95% CI 5%-36%). Stratifying per region, the pooled prevalence in Europe was 15%, whereas in Asia the pooled prevalence was 31%
Arzilli (2022)	Europe, some from Asia, USA, Australia	2010 – 2021	PubMed, Cochrane, PsycInfo	Patients admitted to hospitals	AMR-GNB	Identify prevalence and risk of infection among those colonized	93	Case-control, RCT, cohort study	NA	GNB: Overall prevalence 13.8% Higher prevalence in USA and ASIA, in Europe higher prevalence in southern Europe
Bezabih (2021)	Several	2000 – 2020	PubMed, EMBASE, Google Scholar	Healthy individuals in community settings	ESBL-E. coli	Determine the global prevalence and trends of human faecal colonisation of ESBL-producing E. coli in the community over the past two decades	62	Prospective and cross-sectional studies	29872	The cumulative global pooled prevalence of ESBL-producing E. coli intestinal colonisation was 16.5% (95% CI: 14.3%–18.7%). Prevalence increased from 2.6% in 2003-2005 to 21.1% in 2015-2018. Highest prevalence rates were observed in South-East Asia (27%) and the lowest in Europe (6%).
Bezabih (2022)	Several	2000 – 2021	PubMed, EMBASE, Google Scholar	Healthcare, community settings	ESBL- coli	Compare the global prevalence and trend of intestinal colonisation of ESBL-producing Escherichia coli between healthcare and community settings	133	Cohort and cross-sectional studies	73318	The global pooled prevalence of intestinal colonisation of ESBL-producing E. coli was 21.1% in healthcare settings and 17.6% in community settings. Prevalence increased from 7% in healthcare settings in 2001–2005 to 25.7% in 2016–2020, and from 2.6% to 26.4% in community settings over the same period.
Biehl (2016)	Several	2002 – 2013	Medline	ICU and oncology patients, transplant recipients	ESBL-E	Assess risk factors for colonisation/infection with ESBL-E producing in high-risk patients	43	Observational studies	Not specified	Colonisation rates in high-risk patients varied greatly by geography, with prevalence ranging from 1.3% to 49.0%, depending on the region and patient population.

Bokhary (2021)	Several	Up to June 2019	PubMed, EMBASE, Scopus	International travellers	ESBL-E, CPE, resistant <i>A. baumannii</i> and <i>P. aeruginosa</i>	Investigate the impact of travel on the dissemination of antimicrobial resistance	238	Cohort, case-control, cross-sectional, case series, and case reports	Not specified	The prevalence of ESBL-producing organisms in travellers varied significantly across regions, with many isolates originating from Asia. Carbapenemase-producing <i>Klebsiella pneumoniae</i> was increasingly detected, particularly in medical travellers.
Detsis (2017)	Several	Up to November 2015	PubMed, EMBASE	ICU patients	ESBL-E	Evaluate ICU acquisition rate, risk factors, and risk of infection associated with ESBL-PE colonisation	13	Observational studies	15,045	The ICU acquisition rate of digestive tract colonisation with ESBL-E was 7% (95% CI: 5–10%), with regional variations: 3% in the Americas and Europe, 21% in the Western Pacific.
Dharmapalan (2017)	India	2000 – 2015	PubMed, Scopus, Google Scholar	Pediatric bloodstream infections	ESBL-E/CPE	Review all antibiotic-resistant bacteria in pediatric bloodstream infections in India	89	Observational studies	50,545 blood cultures (14,704 positive)	High rates of resistance to third-generation cephalosporins were observed, especially in <i>K. pneumoniae</i> (62.6%) and <i>E. coli</i> (47.5%). Emerging carbapenem resistance was noted in <i>K. pneumoniae</i> (1%). ESBL-specific results are difficult to extract due to reporting primarily in the form of pathogen-drug combinations.
Flokas (2017)	Several	Up to May 2016	PubMed, EMBASE	Long-term care facility residents	ESBL-E	Estimate colonisation rate of ESBL-producing Enterobacteriaceae among long-term care facility residents	23	Prospective studies	9,775	The pooled prevalence of ESBL-E colonisation among long-term care facility residents was 18% (95% CI: 12–24%). Colonisation rates were 31% in Asia, 18% in Europe, 13% in North America, and 8% in Oceania.
Fulchini (2019)	Switzerland	2000 – 2017	PubMed, MEDLINE, Embase	Various patient settings in Switzerland	ESBL-E/CPE, MRSA, VRE, MDRPA, MDRBA (mcr)	Summarize AMR prevalence across different patient populations in Switzerland and identify surveillance gaps	46	Cross-sectional and cohort studies	Not specified	ESBL prevalence in universal admission screenings was 5–8%, with higher rates (14–21%) in targeted screenings. ESBL prevalence among refugees ranged from 9–24% and returning travellers had very high colonisation rates (68–80%). CPE prevalence was 1–3% in targeted screenings.
Furuya-Kanamori (2020)	Several	2000 – 2019	PubMed, Web of Science, Scopus	International travellers	ESBL-E, CPE	Quantify risk factors and interventions for ESBL and CPO acquisition among travellers	20	Epidemiological (observational) studies	5,253	South Asia had the highest proportion of MRE (ESBL-E/CPE) acquisition (58.7%), followed by Northern Africa (43.9%). Carbapenemase-producing Enterobacteriales were reported in Southeast Asia and the Indian subcontinent.
Granata (2024)	Several	2000 – 2023	PubMed, SCOPUS	Patients and soldiers in conflict zones	ESBL-E/CPE, <i>Pseudomonas aeruginosa</i>	Summarize the prevalence and causes of antibiotic resistance development in armed conflict settings	34	Surveillance and retrospective observational studies	Not specified	High prevalence of ESBL-producing <i>K. pneumoniae</i> and <i>E. coli</i> in conflict settings, with rates above 60% in Iraq and Afghanistan. Carbapenemase-producing organisms, such as <i>K. pneumoniae</i> producing NDM and OXA-48, were reported in Ukraine and Libya, with resistance rates reaching 80% for some carbapenemases.
Hassing (2015)	Several	Up to 2015	EMBASE, Web of Science, Scopus, Cochrane library, PubMed etc	Healthy individual travelling	Multidrug-resistant <i>Enterobacteriaceae</i> (MRE, defined as ESBL-E/pAmp C-E)	Identify risk for colonisation associated with travels	11	Prospective cohort study	2331	Faecal colonisation of MRE varied from 1-12% before travel and acquisition of MRE from 21-51%
Hu (2020)	Several	2014 – 2019	PubMed, EMBASE, Web of Science	Healthy individual	Drug resistant <i>E. coli</i>	Identify prevalence and risk for colonisation	15	Cross sectional	11480	Pooled prevalence 14% (8% among general population and 37% travellers)
Jalilian (2019)	Several		PubMed, EMBASE, Scopus, Web of Science	Pregnant/post-partum women	ESBL-E	Identify global maternal colonisation with ESBL-PE	19	Cross sectional	7352	Pooled prevalence 8%. Africa 15%, South America 6%, Asia 5%, Europe 4%

Karanika (2016)	Several	1978 – 2015	PubMed, EMBASE	Healthy individuals	ESBL-E	Identify prevalence and risk factors	66	Cross sectional	2809	Pooled prevalence of faecal colonisation with ESBL-PE were 14%. West Pacific 46%, Southeast Asia 22%, Eastern Mediterranean 15%, Europe 4%, America 2% Annual increase rate of 5.38%
Konar (2023)	Several countries (primarily African countries)	Up to september 2023	Google Scholar, Scopus, Cochrane, PubMed	HIV-infected patients	CRE, other resistant organisms	Consolidate data on carbapenem resistance among HIV-infected cohorts (scoping review)	15	Cross-sectional and retrospective studies	2365	The prevalence of CRE colonisation in HIV-infected patients was low, with only one study reporting CRE colonisation. The presence of carbapenem-resistant <i>Acinetobacter baumannii</i> (CRAB) was noted in several studies
Leangapichart (2017)	Saudi-Arabia	2002 – 2017	Pubmed, Scopus, and Google Scholar	Pilgrims to Mekka (Hajj)	ESBL	Identify prevalence of major gram-positive and gram-negative AR bacteria isolated in pilgrims or other populations living in the area where pilgrims stay, including Mecca, Mina, and Medina.	31 (17 looked at prevalence)	Cross sectional and cohort	6721	The prevalence of the blaCTX-M gene in rectal samples was 10% before-Hajj compared to 33% after-Hajj AND in another study 7% before-Hajj compared to 34.83% after-Hajj. Across all studies, carbapenem-resistant bacteria were detected in fewer than 10% of <i>E. coli</i> isolates tested but up to 100% in <i>K. pneumoniae</i> and <i>A. baumannii</i> . Colistin-resistant <i>Salmonella enterica</i> , including mcr-1 colistin-resistant <i>E. coli</i> and <i>K. pneumoniae</i> were only detected in the pilgrim cohorts
Loaiza (2023)	Several	2017 – 2022	Science Direct, Redalyc, Scopus, PubMed/Medline, etc.	ICU patients with hospital-acquired infections	ESBL-E/CPO	Review the prevalence of bacteria resistant to antibiotics and the distribution of antibiotic resistance genes in ICU-acquired infections	114	Cross-sectional and cohort studies	Not specified	ESBL-producing <i>K. pneumoniae</i> and <i>E. coli</i> were frequently reported, with ESBL prevalence reaching up to 40% in some studies. Carbapenemase-producing <i>K. pneumoniae</i> and <i>P. aeruginosa</i> were also common, particularly in Asia and Africa. The blaOXA and blaCTX genes were the most prevalent resistance mechanisms
Luo (2023)	Several countries	Up to october 2022	PubMed, Embase, Web of Science, MEDLINE, Cochrane	Haematological malignancy patients	CRE, ESBL-E	Assess prevalence and risk factors for CRE and ESBL colonisation in haematological malignancy patients	32	Cohort, case-control, cross-sectional	21,402	The pooled prevalence of CRE was 21.7% (95% CI: 18.7–24.8), and for ESBL-producing Enterobacteriaceae 19.2% (95% CI: 13.9–24.5). Higher CRE prevalence was observed in South-East Asia (57.4%)
Martischang (2020)	Several countries	1990 – 2018	PubMed, Embase, Cochrane, CINAHL	Household members	ESBL-E	Assess co colonisation and acquisition rates of ESBL-producing Enterobacteriaceae in households	13	Cross-sectional and cohort studies	863 household members	ESBL-PE cocolonisation among household members ranged from 8% to 37%. The pooled co colonisation proportion of clonally related ESBL-PE was 12% (95% CI: 8%–16%). Acquisition rates of clonally related ESBL-PE were 1.56 to 2.03 events per 1,000 person-weeks of follow-up
Moradi (2021)	Several countries	1990 – June	PubMed, Embase, Scopus, Web of Science, Cochrane etc	Pregnant women	ESBL- <i>E. coli</i>	Determine the prevalence of <i>E. coli</i> and ESBL-producing <i>E. coli</i> in pregnant women	19	Cross-sectional and retrospective studies	9,200	The pooled prevalence of ESBL-producing <i>E. coli</i> in pregnant women was 34% (95% CI: 24–43%), with higher prevalence in Asia (50%) and Africa (30%). Among pregnant women with HIV, the prevalence was 9%
Muzembo (2022)	Travel to India from multiple countries (Canada, Europe, Japan, USA)	2000 – 2021	PubMed, EMBASE, Web of Science, Google Scholar, grey literature	International travellers to India	ESBL- <i>E. coli</i>	Assess acquisition rates of ESBL-EC among international travellers visiting India	17	Cross-sectional and cohort studies	220 ESBL cases	The pooled ESBL-EC colonisation rate among travellers was 72%, with the CTX-M-15 enzyme being the most commonly produced. Colonisation rates were more or less consistent across studies
Osei Sekyere (2021)	Several	Up to september 2020	PubMed, Web of Science, Cochrane etc.	Pregnant women, neonates, infants (<5 years)	Carbapenem /polymyxin-resistant GNB	Investigate the molecular epidemiology and clinical outcomes of CR and PR GNB infections	73	Cohort and cross-sectional studies	49154 infants 1892 pregnant women	CR-GNB prevalence (isolation rate) in toddlers, infants, and neonates was 23.3%. In pregnant women, the isolation rate was 15.1%. Carbapenem resistance exceeded 50% in eight countries, with some settings, including Ghana, Greece, Japan, Poland, and Taiwan, reporting 100% resistance

Peters (2019)	Several	2000 – 2019	PubMed, MEDLINE, Web of Science, CINAHL	Healthcare personnel	ESBL, CPO (VRE, MRSA, MDR-GNB)	Assess the occupational infection risk posed by ESBL and CPO among healthcare personnel	22	Primarily cross-sectional studies	Not specified	ESBL prevalence ranged from 2.6% to 48.5%. CPO was studied in four studies, but no positive findings were reported in hospital settings
Prevel (2019)	Several	Up to february 2019	MEDLINE	ICU patients	ESBL-E	Investigate the utility of faecal colonisation screening of ESBL-E for guiding ICU infection prevention measures	25	Not a commentary or a review or an erratum	Not specified	Reported ESBL-E colonisation prevalence ranged from 0.97% to 28.2% across studies. Screening did not significantly reduce cross-transmission rates
Righi (2023)	Several	2011 – 2022	Medline, Embase, Cochrane	Hospitalised surgical patients	Extended-spectrum cephalosporin-resistant Enterobacteriales (ESCR-E)	Evaluate risk of postoperative infections in ESCR-E carriers vs non-carriers	9	Observational studies	7219	Pooled colonisation rate of ESCR-E was 13.7%. Postoperative infection risk was higher in ESCR-E carriers (36%) vs non-carriers (13%). SSIs: 28% vs 17%
Vink (2020)	Several	Up to september 2019	PubMed	Hospitalised patients	ESBL-E, MDR-GNB	Assess colonisation and acquisition rates of ESBL-E and MDR-GNB in hospital settings	28	Cohort, case-control studies, intervention studies and quasi-experiments	Not specified	Pooled prevalence of ESBL-E on hospital admission was 7.91%, and the acquisition rate was 3.73% in a subset of eight papers with patients from Europe and North America
Voor (2020)	Several	Up to june 2019	Embase, Medline, Ovid, Cochrane, Scopus, Cinahl etc.	International travellers	Multidrug-resistant Enterobacteriales (MDR-E), CPE	Identify colonisation rates of MDR-E among returning travellers and leading risk factors	22	Prospective cohort studies	Not specified	Prevalence of MDR-E among travellers was highest among those returning from Southern Asia (71%) and Northern Africa (42%). CPE prevalence was rare, reported in only 5 studies
Wuerz (2020)	Several	2000 – 2018	PubMed, Embase, MEDLINE, Cochrane Library, etc.	Travellers (asymptomatic)	ESBL-E	Assess the association between antimicrobial use during travel and ESBL-PE acquisition	15	Prospective cohort studies	5283	Prevalence of ESBL-E colonisation among travellers was 14%, with the highest prevalence among travellers returning from Southern Asia (71%) and Northern Africa (42%)

ESBL-E: extended spectrum beta-lactamase producing Enterobacteriales (which includes Enterobacteriaceae); CPO: carbapenemase producing organisms; CPE: carbapenemase producing Enterobacteriales (which includes Enterobacteriaceae); CRE: carbapenem-resistant Enterobacteriales (which includes Enterobacteriaceae); CRAB: carbapenem-resistant Acinetobacter baumannii; CRPA: carbapenem-resistant Pseudomonas aeruginosa; MDRAB: multidrug-resistant A. baumannii; XDRAB: extensively drug-resistant A. baumannii; IRAB: imipenem-resistant Acinetobacter baumannii; 3GCRES: third generation cephalosporin resistant enterobacteriales; pAmp C-E: pAmp C-producing Enterobacteriales; CRKP: Carbapenem-resistant Klebsiella pneumoniae, GNB; Gram-negative bacteria

Table 6. Overview of characteristics and findings of studies from the Nordic countries and the Netherlands on prevalence of ESBL/CPO in asylum seekers and refugees and patients hospitalised abroad

Author (Year)	Country	Study period	Study design	Setting/ population	Pathogens	Study objective	Screening type	Screening site	No. of screened patients	No. of positive patients	Authors' conclusion
Aro (2018)	Finland	2010 – 2017	Retrospective Cohort study	Asylum seekers	ESBL (MRSA, VRE)	Investigate the prevalence of various MDR bacteria among asylum seekers/refugees hospitalised in Finland	Admission screening	Rectal swab	447		Colonisation was common among asylum seekers and refugees arriving from current conflict zones. Of 447 asylum seekers and refugees (Iraq: 46.5%; Afghanistan: 10.3%; Syria: 9.6%, Somalia: 6.9%); 45.0% were colonised by MDR bacteria: 32.9% had ESBL-E and 0.7% carbapenemase-producing Enterobacteriaceae (CPE), 0.4% (MRPA) and 0.4% multiresistant MRAB. Young age (< 6 years old), short time from arrival to first sample, and prior hospitalisation outside Nordic countries were riskfactors of colonisation
Hertting (2021)	Sweden	2015 – 2016	Cohort study	Hospitalised asylum seekers	ESBL (and MRSA/other infectious diseases)	Identify hospitalizations due to infectious diseases among asylum seekers compared to resident population	Screening during hospitalisation	N/A	263		Almost one-third of the screened AS in this study were carriers of ESBL-producing bacteria or MRSA
Ravensbergen (2016)	Netherlands	Up to september 2015	Retrospective cohort study	Asylum seekers	ESBL (other MDRO)	Resistant microorganisms in asylum seekers with possible consequences for public health and infection control	Screening after hospitalisation abroad		273		A colonisation rate of 31% for multi-drug-resistant microorganisms (MDRO) was observed, with ESBL-expressing E. coli (n = 20) being the most common MDRO. No colonisation of CPE was found
Ravensbergen (2017)	Netherlands	2014 – 2015	Cohort study	Asylum seekers	ESBL-E (MRSA)	Describe MRSA and MDRE rate among asylum seeker compared to the general patient population	Screening after hospitalisation abroad		1071	859	The study shows significantly higher rates of MDRE among the asylum seekers' population than the general patient population. These differences justify screening of the asylum seekers' population at admission in the hospital as these organisms may be a threat to the patient and transmission in the hospital should be prevented. More than 21% of the asylum seekers were carrier of MDRE, most of them producing ESBL (20.3%). 5.1% of the general patient population was MDRE carrier
Kajova (2021)	Finland	2010 – 2019	Cohort study	Hospitalised patients abroad. Adults and children	ESBL – PE and other MDR	MDR bacterial colonisation among patients transferred directly from hospitals abroad to Helsinki University Hospital.	Screening after hospitalisation abroad		698	208	Colonisation by MDR bacteria was common among patients transferred from foreign hospitals. Region of hospitalisation, ICU treatment and antibiotic use were predisposing factors. Colonisation rates proved highest for transfers from Asia (71.9%) and lowest for those within Europe (18.9%). Of all patients 29.8% were colonised; among those, 78.4% carried ESBL-PE, 13.5% MDR Acinetobacter species, 12.0% MRSA, 12.0% VRE, 6.7% carbapenemase-producing Enterobacteriaceae, and 5.8% MDR Pseudomonas aeruginosa; 46 strains tested carbapenemase gene-positive

Kajova (2022)	Finland	2010 – 2019	Cohort study	Hospitalised patients abroad. Adults	ESBL, MRSA, VRE	Gather country-specific data on the risks for patients hospitalized abroad.	Screening after hospitalisation abroad		1772		After hospitalization in European countries, ESBL-PE colonisation was relatively common (12.5%), while other MDROs proved less frequent (<5%). The MDRO rates were highest in the east, followed by southern, western and northern subregions, in this order. Antibiotic treatment and short time since hospitalization abroad increased the risk of MDRO colonization. Clear differences between countries and regions were revealed, with highest rates in the east and the south
Khawaja (2017)	Finland	2010 – 2013	Cohort study	Hospitalised patients abroad. Adults and children	ESBL, MRSA, VRE	MDR colonization among patients hospitalized abroad in various geographic regions.	Screening after hospitalisation abroad		1122	333	MDR colonization rates were higher for those hospitalized in the (sub)tropics (55%) compared with temperate zones (17%). For ESBL-PE the percentages were 50% versus 12%, CPE 3.2% versus 0.4% and MRSA 6.6% versus 2.4%. Colonization rates proved highest in those returning from South Asia (77.6%), followed by those having visited Latin America (60%), Africa (60%) and East and Southeast Asia (52.5%). Destination, interhospital transfer, short time interval to hospitalization, young age, surgical intervention, residence abroad, visiting friends and relatives, and antimicrobial use proved independent risk factors for colonization.
Westerholt (2021)	Denmark	2016 – 2019	Cohort study	Hospitalised patients abroad. Adults and children	ESBL, MRSA, VRE	Colonisation prevalence and geographical risk stratification for patients with previous contact with healthcare abroad (outside nordic contries) within 6 months	Screening after hospitalisation abroad		2849	120	This study detected a total of 120 resistant isolates, with the highest detection rate for CPO (1.5%), followed by MRSA (1.3%) and VRE (1.1%). Southern and Western Asia were overrepresented travel destinations in positive screening sets (41%).

MRSA: methicillin-resistant *Staphylococcus aureus*; VRE: vancomycin-resistant *Enterococcus* ESBL-E: extended spectrum beta-lactamase producing Enterobacterales (which includes Enterobacteriaceae); CPO: carbapenemase producing organisms; CPE: carbapenemase producing Enterobacterales (which includes Enterobacteriaceae); CRE: carbapenem-resistant Enterobacterales (which includes Enterobacteriaceae); CRAB: carbapenem-resistant *Acinetobacter baumannii*; CRPA: carbapenem-resistant *Pseudomonas aeruginosa*; MDRA: multidrug-resistant *A. baumannii*; XDRAB: extensively drug-resistant *A. baumannii*; IRAB: imipenem-resistant *Acinetobacter baumannii*; 3GCRE: third generation cephalosporin resistant enterobacterales; pAmp C-E: pAmp C-producing Enterobacterales; CRKP: Carbapenem-resistant *Klebsiella pneumoniae*; MDRE: multidrug-resistant Enterobacteriaceae.

4. Associated factors

Systematic reviews

We included 24 systematic reviews (7,8,22,28-30,32,34,36,38,42,46,48,57-67), of which 22 reviews reported on factors associated with infection and colonisation with ESBL-/carbapenemase-producing Enterobacterales, and five reporting on carbapenemase-producing *Acinetobacter* spp. or *Pseudomonas aeruginosa* (29, 58-60,67). The studies are summarized in Table 7.

Several of the included systematic reviews found association between hospitalisation, especially prolonged hospitalisation and ICU-stay and increased risk of colonisation with ESBL- or carbapenemase-producing Enterobacterales, among hospitalised patients (22,28,30,46,48,57,59,62,63-66). Previous antibiotic treatment among hospitalised patients was also associated with increased risk of colonisation with ESBL- or carbapenemase-producing Enterobacterales (22,28,30,42,46,48,57-59,63-67). However, whether the associations were statistically significant varied in the included studies. De Blasiis et al. and Sulis et al. found that previous antibiotic treatment was associated with colonisation with carbapenem-resistant *Acinetobacter baumannii* (CRAB) among ICU-patients (58) and hospitalised patients (67), the same was shown for CRAB-infection in hospitalised patients by Deshwal et al. (59). Other associated factors were mechanical ventilation and surgery (46,59, 60,62,64,65), comorbidities (57,66) and central venous catheter (62,64). Flokas et al. investigated residents of long-term care facilities (LTCF) and found that recent antibiotic use, previous hospitalisation, history of invasive procedures, previous ESBL colonisation or infection, history of urinary tract infection and urinary catheter use were associated with ESBL colonisation (32).

The included systematic reviews focusing on international travellers found that antibiotic resistant *Enterobacterales*, including ESBL/carbapenemase-producers, mostly originated from Asia, especially south-east Asia, and Northern-Africa, followed by Sub-Saharan Africa and Central and South America (7,8,29,33,34,36,45,51,52). Bokhary et al. found that medical travellers have around twice the odds of detected MDR bacterial isolates than other travellers (OR = 1.99, $p < 0.001$), and that nearly all of the AMR strains of *A. baumannii* and *Pseudomonas aeruginosa* were associated with medical travellers (29). Furuya-Kanamori et al. (34) found the strongest risk factors of colonisation to be antibiotic use while travelling (OR 2.4; 95% CI 1.9–3.0) and traveller's diarrhoea (OR 1.7; 95% CI 1.3–2.3). Backpacker travellers had a 50% (OR 1.5; 95% CI 1.2–1.8) increased odds of acquiring MRE compared to other types of travellers. They also found that 2.2% (50/2276) of the isolates had carbapenem-resistant genes, mainly identified from travellers returning from Southeast Asia and the Indian subcontinent, while Hassing et al. (7) only found two studies reporting on carbapenemase-producing bacteria (n=4).

One systematic review did not find contact with pet to be associated with colonisation or infection with carbapenem-resistant Enterobacterales (CRE) or Enterobacterales resistant to third generation cephalosporins (3GCRE) (61).

Primary studies from the Nordic countries and the Netherlands

We included 14 primary studies on travellers and the acquisition of ESBL-E/CPE, and carbapenemase-producing *Acinetobacter* spp. or *Pseudomonas aeruginosa*. Four of the studies (9,78,85,93) were included in one of the systematic reviews (34) and are not further mentioned. Ten primary studies on travellers (68-74,89,91,96) are summarised in Table 8. One study by D'Souza et al. (70) was based on the same population as Arcilla et al. (68).

Six studies on healthy travellers found high rates of ESBL-E colonisation after travel to Asia and Northern Africa (68,69,74,89,91,96). Arcilla et al. also found that travels to Australia or New Zealand was associated with ESBL-E colonisation (68). Kajova et al. investigated patients admitted to a Finnish hospital and found the highest MDRO rates (incl. ESBL-E/CPE) in patients who had been hospitalised or underwent major invasive procedure in Bulgaria (38.1%), Cyprus (31.8%) and the Russian Federation (26.4%). Travel to Eastern Europe was associated with the highest prevalence of both MDRO colonisation in general and ESBL-E specifically (71). One study looked at students travelling to India and found that 35/45 students tested positive on a special resistance gene during their stay (72).

Table 7. Overview and findings of systematic reviews on associated factors of ESBL/CPO colonisation/infection.

Author (Year)	Country	Search period	Databases	Setting/ population	Pathogens	Study objective	No. studies incl.	Type of studies incl.	No. of patients	Authors' conclusion
Abera (2023)	Europe, Asia, Africa	2016 – 2022	PubMed, Google Scholar and Web of Science	Hospitalised patients throughout the world	ESBL-E/CPE	To assess colonisation rate and risk factors of ESBL-PE and CRE colonisation among hospitalized patients.	20	Cross sectional, case-control and cohort	ESBL: 11647 CRE: 8733	Prolonged hospitalization/admission within the last 3, 6 or 12 months was linked to CPE colonization. History of antibiotic treatment in the last 3 and 6 months was found to be a risk factor for ESBL-PE colonisation – not significant
Bar (2023)	Europe (Middle East, Far East and overseas countries were included when relevant)	Up to March 2022	PubMed, Embase, Cochrane Library	Hospitalised patients	CPE	Identify additional risk factors for CPE colonisation/infection to improve screening protocols	19	Case-control, cross-sectional, descriptive studies	N/A	Previous/current hospitalization in ICU (1 week) and 20–28 days in other wards was significant CPE risk factors. Previous or current antimicrobial therapy, especially broad-spectrum antibiotics, was also significant. Comorbidities and invasive procedures have an unmeasurable impact and travel abroad can be considered a risk factor in low-prevalence countries.
Biehl (2016)	N/A	2002 – 2013	Medline	ICU patients, patients in hematology and oncology wards, transplant recipients	ESBL-E	Review the literature to assess risk factors for colonisation and infection with ESBL-producing Enterobacteriaceae in high-risk patients	43 (6 studies on risk factors for colonisation)	Observational studies	N/A	The most frequently reported risk factor for both, colonisation/infection with ESBL-E, was prior antibiotics exposure. In addition, prior contact with health care seems to be particularly relevant. OR for prior exposure to third-generation cephalosporins (OR = 5.96) and transfer from another ICU (OR = 2.56) were particularly impactful.
Bokhary (2021)	Several	Up to June 2019	PubMed, EMBASE, Scopus	International travellers	26 drug-resistant bacterial species, including ESBL-E, CPE, resistant <i>A. baumannii</i> and <i>P. aeruginosa</i>	Investigate the impact of travel on the dissemination of antimicrobial resistance	238	Cohort, case-control, cross-sectional, case series, and case reports	N/A	AMR <i>E. coli</i> mostly originated from Central/South America (25.49%), and Asia (21.41%; excluding West Asia). Resistant <i>K. pneumoniae</i> , incl. carbapenem-resistance, mostly originated from Asia. Medical travellers had around twice the odds of detecting MDR bacterial isolates than other travellers. Nearly all of AMR strains of <i>A. baumannii</i> / <i>Pseudomonas aeruginosa</i> were associated with medical travellers.
De Blasiis (2024)	Several countries	Up to February 2023	PubMed, Scopus, Web of Science	ICU patients	CRAB, MDRAB, XDRAB	Evaluate exposure to antibiotics on isolation of resistant <i>Acinetobacter baumannii</i> in ICU patients	25	Cohort, case-control studies	40,667	Significant association with CR/MDR AB isolation for previous exposure to aminoglycosides (OR: 1.98), carbapenems (2.64) third generation cephalosporins (1.36), glycolylcyclines (2.42), and nitroimidazoles (4.11).
Deshwal (2023)	Several	2000 – 2021	PubMed, OVID	Hospitalised patients	MDRAB, XDRAB, CRAB, IRAB	Identify risk factors for resistant <i>Acinetobacter baumannii</i> infection relative to controls	38	Case-control, cohort studies	60,878	Factors associated with CRAB infection included prior use of amikacin (OR 4.94), previous carbapenem exposure (OR 4.91), pneumonia (OR 4.71), mechanical ventilation (OR 3.46), prior use of piperacillin-tazobactam (OR 2.92). For IRAB infection, ICU stay (OR 3.51), carbapenem exposure (OR 2.94), and surgery (OR 2.90).
Detsis (2017)	Several	Up to November 2015	PubMed, EMBASE	ICU patients	ESBL-E	Evaluate ICU acquisition rate, risk factors, and risk of infection associated with ESBL-PE colonisation during ICU stay	13	Prospective and retrospective observational studies	15,045	Factors associated with ESBL-E colonisation during ICU stay included previous antibiotic use (RR 1.65), carbapenem use (RR 2.13), previous hospitalization (RR 1.57). Colonized patients were at significantly higher risk of developing an ESBL-E infection (RR 49.6).

Flokas (2017)	Several (Europe, North America, Asia, Oceania)	Up to May 2016	PubMed, EMBASE	Long-term care facility residents	ESBL-E	Estimate the colonisation rate of ESBL-producing Enterobacteriaceae among long-term care facility residents	23	Prospective studies	9,775	Factors associated with ESBL colonisation included recent antibiotic use (OR = 2.06, 95% CI 1.78–2.38), past hospitalisation (OR = 1.50, 95% CI 1.04–2.15), Invasive procedures (OR = 2.79, 95% CI 1.66–4.70), history of UTI (OR = 2.66, 95% CI 1.76–4.01), Urinary catheter use (OR = 2.55, 95% CI 1.29–5.04), history of ESBL-PE colonisation or infection (OR = 6.77, 95% CI 1.33–34.62)
Furuya-Kanamori (2020)	Europe, USA, Japan, Australia	2000 – 2019	PubMed, Web of Science and Scopus	International, healthy travelers	ESBL-E, CPE	Quantify the risk factors and interventions for reducing the risk of MRE acquisition among international travellers.	20		5253 travellers from high-income countries	Risk factors for MRE colonisation were travel to South Asia/Northern Africa, Inflammatory bowel disease, use of antibiotics, traveller's diarrhoea and contact with the healthcare overseas Vegetarians (OR 1.4) and backpackers (OR 1.5) were also at increased odds of MRE colonisation. 2.2% of the isolates were found with carbapenem-resistant genes, mainly identified from travellers returning from Southeast Asia and Indian subcontinent.
Gao (2024)	Mainly China, Brazil, USA, Italy	Up to 2023	PubMed, Embase and Web of Science	Transplant patients	Carbapenem-resistant gram-negative bacteria (CRGNP, incl. CRE, CPE, CRAB, CRPA)	Identify risk factors associated with CRGNB infection and colonisation in transplant patients	23	Mainly case-control and cohort studies	13 511	Significant risk factors for CRGNB-infection: prolonged mechanical ventilation, combined transplantation, re-operation, pre-transplantation CRGNB colonisation and the mean length of post-transplantation ICU stay The presence of re-transplantation and carbapenem use before transplantation were associated with a significantly increased risk of CRGNB colonisation
Hackmann (2022)	Mainly USA and Europe	Up to 2020	Not listed	Studies describing risk of AMR after contact with animals	CRE, 3GCRE	Examine if contact with animals is associated with risk of AMR-colonisation /infection	13	Cohort and case-control	10472 cases	Contact with pet was not found as a risk factor for CRE or 3GCRE
Hassing (2015)	Northern and western Europe, Australia and the United States	Up to 2015	EMBASE, Medline, Web of Science, Scopus, Cochrane library, PubMed etc	Healthy travellers	Multidrug-resistant <i>Enterobacteriaceae</i> (MRE, defined as ESBL-E/pAmp C-E)	Identify risk for colonisation associated with travelles	11	Prospective cohort study	2331	Travel to southern Asia posed the highest risk (range: 29–88%), followed by other Asian countries (18–67%) and Northern Africa (range: 31–57%). Acquisition of MRE after travelling to sub-Saharan Africa (range: 0–49%) or South and Central America (range: 0–33%) was less frequent Other risk factors for acquiring MRE were age, use of antibiotics during travel (beta-lactam use) and gastroenteritis or other gastrointestinal symptoms
Hu (2020)	England, Gambia, Germany, Netherlands, Cyprus, Singapore, Sweden, Tanzania	2014 – 2019	PubMed EMBASE, Web of Science	Healthy travellers and pig farmers	Drug resistance <i>Escherichia coli</i>	Investigate risk factors associated with colonisation of drug-resistant commensal <i>E. coli</i> in the recent five years	15	Cohort, case-control, cross-sectional	11480	Traveling to India was the only risk factor that all studies reported to be significantly associated with fecal colonisation of drug-resistant <i>E. coli</i> . Other risk factors: antimicrobial use within the previous 12 months (OR 1.84), diarrhea symptoms (OR 1.56), and vegetarian diet (OR 1.60)
Jeon (2023)	Several	2016 – 2021	Medline, EMBASE, Cochrane CINAHL etc	Patients admitted to hospital	CPO	Identify existing clinical predictions tools	3	Retrospective cohort	60	Identified risk factors for colonisation/infections were previous and recent hospital admission. Other risk factors steamed from health care were identified source as CV-catheter use, recent surgery, mechanical ventilation, stay in ICU

Karanika (2016)	Several	1978 – 2015	PubMed, EMBASE	Healthy individuals	ESBL-E	Prevalence of ESBL class A colonisation among healthy patients and assess the factors that are associated with the colonisation status	66	Prevalence studies?	28 909	Based on 3 studies on 182 individuals, those who traveled to India were more likely to be colonized with ESBL compared with those who traveled to any other destination (RR = 2.4). Travel to Africa did not increase the risk for ESBL colonisation (RR = 0.94)
Kedisaletse (2023)	African countries	2000 – 2022	PubMed, Scopus and Web of Science	Mainly hospitalised patients	CRE	Identify epidemiology of CRE infections and colonisation in Africa and identification of risk factors for CRE infection and colonisation, as well as outcomes of CRE	169 (16 reported on risk factors)	Mainly cross-sectional	15666	Risk factors for CRE/CPE was previous antibiotic exposure and previous hospitalization. Risk factors for CRE infection were the use of indwelling devices, previous antibiotic exposure and admission to ICU, previous hospitalisation and length of hospital stay. One study reported surgical procedures as a risk factor
Li (2017)	Several countries (China, Italy, India, Brazil, Norway, etc.)	2000 – 2016	PubMed, Web of Science, EBSCO, Cochrane; CNKI, CBM, Wanfang	NICU patients (neonates)	ESBL-E	Identify factors associated with infection and/or colonisation with ESBL-producing bacteria in the NICU	14	Case-control, cohort studies	2003	Factors associated with ESBL infection/colonisation included low birthweight (SMD=1.17), gestational age (SMD=1.36), Caesarean delivery (OR=1.76), parenteral nutrition (OR=7.51), length of stay in the NICU (SMD=0.72), mechanical ventilation (OR=4.8), central venous catheter use (OR=2.85), continuous positive airway pressure (OR=5.0), endotracheal intubation (OR=2.82), malformations (OR=2.89), and previous antibiotic use (OR=6.72).
Li (2020)	Several (13/30 was China)	Up to October 2018	PubMed, EMBASE, OVID, ClinicalKey, CNKI, CBM, Wanfang Database, CHKD	Hospital patients	CRKP	Identify factors associated with CRKP infection through a meta-analysis	30	Case-control studies	5075	Factors associated with CRKP infection, based on meta-analysis results, include ICU admission (OR 3.25), carbapenem exposure (OR 3.99), mechanical ventilation (OR 2.91), central venous catheterisation (OR 2.93), glycopeptide exposure (OR 3.08), quinolone exposure (OR 1.75), and nasogastric intubation (OR 2.38). Other associated factors include surgery, indwelling catheter, and β -lactam/ β -lactamase inhibitor exposure (OR 2.28).
Ling (2022)	Europe, USA, New Zealand, Asia, South America	Up to April 2021	PubMed, EMBASE, Scopus	Adults. Community, discharged patients, travellers	ESBL-E	Estimate the duration of colonisation in the community/ house-hold transmission	26	Cross-sectional, cohort studies	2505	All the travel-related studies had the highest prevalence of participants returning from Asian countries. ESBL-E colonisation was significantly lower at all studied time points in travelers compared to discharged hospital patients.
Luo (2023)	Several countries	Inception–October 2022	PubMed, Embase, Ovid MEDLINE, Cochrane etc	Haematological malignancy patients	CRE, ESBL-E	Assess prevalence and factors associated with CRE and ESBL colonisation in haematological malignancy patients	32	Cohort, case-control, cross-sectional	21,402	Factors associated with CRE colonisation were prior tigecycline use (OR 3.99), chemotherapy (OR 2.45), neutropenia (OR 1.88), and acute myeloid leukaemia (AML; OR 1.86). Other factors included prior use of carbapenems (OR 1.84) and penicillin (OR 1.72). For ESBL colonisation, prior antibiotic exposure was the most significant associated factor (OR 4.90).
Mohd (2019)	Italy, USA, Thailand, Taiwan	Inception to April 2018	Medline, Embase, CINAHL, Cochrane Database of Systematic reviews	Hospitalised patients	ESBL-E	To identify and critically appraise clinical prediction models for ESBL-EKP colonisation or infection in hospitalized patients.	4	Retrospective case-control and cohort studies	N/A	The most commonly identified predictors were previous antibiotic use, previous hospitalization, and transfer from another healthcare facility. Other predictors included invasive procedures (urinary catheterization), prolonged hospitalization, immunosuppression, older age, and comorbidities.

Osei Sekyere (2021)	Several	Up to September 2020	PubMed, Web of Science, ScienceDirect, Cochrane etc.	Pregnant women, neonates, infants (<5 years)	Carbapenem-resistant and polymyxin-resistant gram-negative	Investigate molecular epidemiology and clinical outcomes of CR and PR GNB infections	73	Cohort and cross-sectional studies	49,154 infants, 1892 pregnant women	Common risk factors for colonisation and infection include previous or ongoing antibiotic therapy, prolonged hospitalization, mechanical ventilation, preterm delivery, and low birth weight.
Prevel (2019)	Several	Up to February 2019	MEDLINE	ICU patients	ESBL-E	Investigate the utility of fecal colonisation screening of ESBL-E for guiding ICU infection prevention measures	25	Not a commentary or a review or an erratum	Not specified	Risk factors for colonisation include previous antibiotic use, hospitalisation, and ICU stay.
Sulis (2022)	Several	Up to 2020	Embase, Ovid Medline, Scopus, Cochrane Database, ClinicalTrials.gov	Inpatients or outpatients	Multidrug-resistant organisms (MDROs, incl. CRAB, CRE, CRPA, ESBL-E)	To systematically review and estimate associations between prior antibiotic exposure across WHO AWaRe categories and isolation of critical and high-priority MDROs	349	Case-control, cohort, or interventional studies	Not specified	Prior use of several Watch-group antibiotics was significantly associated with infection/colonisation with CRAB, CRE, and CRPA. Carbapenems were most strongly associated with CRAB (OR=2.2), CRE (OR=2.5), and CRPA (OR=3.2). Use of any antibiotic/class was significantly associated with ESBL-E, with monobactams (OR=2.9), 3GC (OR=2.5), and 4GC (OR=2.4) showing the strongest associations.

ESBL-E: extended spectrum beta-lactamase producing Enterobacterales (which includes Enterobacteriaceae); CPO: carbapenemase producing organisms; CPE: carbapenemase producing Enterobacterales (which includes Enterobacteriaceae); CRE: carbapenem-resistant Enterobacterales (which includes Enterobacteriaceae); CRAB: carbapenem-resistant *Acinetobacter baumannii*; CRPA: carbapenem-resistant *Pseudomonas aeruginosa*; MDRAB: multidrug-resistant *A. baumannii*; XDRAB: extensively drug-resistant *A. baumannii*; IRAB: imipenem-resistant *Acinetobacter baumannii*; 3GCRE: third generation cephalosporin resistant enterobacterales; pAmp C-E: pAmp C-producing Enterobacterales; CRKP: Carbapenem-resistant *Klebsiella pneumoniae*, GNB; Gram-negative bacteria

Table 8. Overview and findings of primary literature from the Nordic countries and the Netherlands on travellers and risk of ESBL/CPO colonisation/infection.

Author (Year)	Country	Study period	Study design	Pathogens	Setting/ population	Study objective	Screening type	Screening method	No. of screened persons	No. of positive before travel	No. of positive after travel	Authors conclusion
Arcilla (2020)	Netherlands	2012 –2013	Cross-sectional	ESBL-E (E.coli)	Dutch travellers	Investigate the prevalence of and risk factors for ESBL-E colonisation in travellers before and after intercontinental travel.	Before and after travel	Faecal swab	2001	122 (6,1%)	585	Two major determinants for ESBL-E colonisation prior to travel: travel outside of Europe in the past 12 months and antibiotic use (attributable risk 39.8% versus 14.9%). Travelled to Eastern Asia, Northern Africa and Australia or New Zealand were at increased risk for ESBL-E colonisation prior to travel. Returning travellers from Western Africa, Southern Asia and Western Asia to be at increased risk for <i>bla</i> CTX-M-15 acquisition and returning travellers from Central- and Eastern Asia to be at increased risk for <i>bla</i> CTX-M-14/18 acquisition.
Davies (2022)	Netherlands		Cohort	ESBL-E	Dutch travellers	Compare the (dynamics in) microbiome between travellers who acquired MDR-E during travel and those that did not	Before and after travel	Faecal swabs	179	11	103 (57,5%)	103 (57.5%) out of the 179 travelers to South Asia, Southeast Asia, North Africa and East Africa, who were negative for ESBL-E prior to travel, acquired ESBL-E during their trip. The vast majority of strains were identified as <i>E. coli</i> (136/148, 91.9%)
D'Souza (2021) Same study population as Arcilla (2020)	Netherlands	2012 –2013	Cohort	AMR genes	Dutch travellers	Combine NGS, metagenomics, and statistical modeling to investigate the abundance, diversity, function, context and acquisition of AMR genes in travellers	Before and after travel	Faecal swabs	190	N/A	N/A	International travel is a significant gut resistome perturbation and highlights the extent of AMR gene acquisition. We found the acquisition of previously unknown, functionally discovered AMR genes, increased AMR gene abundance, and increased resistome α -diversity in the post-travel samples. We also observed AMR gene colocalization with mobile genetic elements and identified travel destination-specific resistome signatures.

Kajova (2022)	Finland	2010 –2019	Retrospective cohort	MDRO (incl. ESBL-E/ CPE, MDRAB, MDRPA)	Hospitalised patients	Analysis of data on patients screened in Finland within a year after treatment and/or a major invasive procedure at hospitals in other European countries.	On admission (if 24-hour hospitalization or medical procedures in a European hospital (excl. Finland) within 12 months)	Stool specimens or rectal swabs	1772	N/A		ESBL-E 12.5%, ESBL <i>K. pneumoniae</i> 2.8%, MDRAB 0.9%, MDRPA 0.7% and CPE 0.6%. 7.8% of the entire study population were colonized only by ESBL <i>E. coli</i> strains. Highest MDRO rates were seen for Bulgaria (38.1%), Cyprus (31.8%) and the Russian Federation (26.4%). Eastern Europe showed the greatest risk of colonisation by MDRO and ESBL-PE. ICU-treated vs. non-ICU-treated patients: 24.5% vs 15.4%, odds ratio 1.8. Destination country and antibiotic use was independently associated with MDRO colonisation; increasing timespan from hospital discharge to screening showed a negative association
Kamenshchikova (2021)	Netherlands	2017	Cohort	AMR genes	Health students from Netherlands, Canada, Colombia and Thailand travelling to India	Incidence of AMR in a particular travellers' group, and how these travellers give meaning to AMR.	During educational stay in India	Faecal swabs	45	5	35	During the stay in India, 35 students tested positive for <i>bla</i> _{CTX-M} genes leading to a total positivity rate for these genes of 78%, which is a significant increase ($p < 0.001$). Thirty-two of 45 students (68%) acquired a new or additional type of <i>bla</i> _{CTX-M} gene.
Kantele (2020)	Finland	2009 –2010	Cohort	ESBL-E	Finnish travellers	Study the clinical significance of travel-acquired ESBL-PE	Before and after travel	Faecal swabs	430	N/A	90 (21%)	A large proportion of imported ESBL-PE strains qualify molecularly as presumptive intestinal or extraintestinal pathogens suggests that more travel-acquired ESBL-PE may cause infections than has been recognized previously
Ljungquist (2020)	Sweden	2018	Cross-sectional cohort	ESBL-E	Swedish travellers	Investigate prevalence and characteristics of colonisation in travellers from Sweden compared to colonisation 10 years ago.	Diagnostic faecal cultures	Faecal cultures	303	N/A	84 (28%)	The prevalence of 28% was slightly higher than in an investigation in a similar population 1 decade earlier (24%), but the difference was not statistically significant. ESBL-E prevalence was highest for travellers from Africa (54%), Asia (45%), and North America and the Caribbean (22%)
Paltansing (2013)	Netherlands	2011	Cohort study	ESBL- E	Dutch travellers. Adults	Investigate risk of MDR-E in travellers and the persistence of intestinal colonization and possible spread to household contacts 6 months after the travelers returned.	Before and after travel	Faecal swabs	370	32	113 (30.5%)	16.8% still carried MDR-E 6 months after return. The highest ESBL-E acquisition rates were identified among participants who visited countries in Asia: South Asia (73%) and East Asia (67%). Participants traveling to Asia were more likely to return with ESBL-E colonization after a self-arranged trip (OR 1.7) or living in hostels/lodges (OR 1.9). The median length of stay abroad was 21 days (6–90 days). The most common reason for travel was vacation.

Reuland (2016)	Netherlands	2016 –2018	Cohort study	ESBL-E CIPR-E CPE	Dutch travellers. Adults	Investigated the rate of and risk factors for travel-related acquisition of different resistant Enterobacteriaceae	Before and after travel	Faecal swabs	455			Colonization with resistant strains (ESBL-E, CIPR-E) after travel to (sub)tropical areas, especially travel to Asia was detected in a large proportion of Dutch travellers. This included ESBL-E, CIPR-E and even one CR-E was detected. Independent risk factors were travel to Asia, and travellers diarrhea in combination with the use of antibiotics.
Vading (2016)	Sweden		Cohort study	ESBL-E	Swedish travellers. Adults	Molecular features of and risk factors for travel-acquired EPE	Before and after travel	Faecal swabs	175		56 (32%)	No carbapenemase-producing Enterobacteriaceae were found. During 10–26 months of follow-up, no clinical infections were observed. Colonization rates varied by visited region: the Indian subcontinent, 49.2%; northern Africa, 44.0%; South-East Asia, 19.1%; and Turkey, 9.5%. Travellers' diarrhoea (OR 2.5, P=0.04) or antimicrobial treatment during the trip (OR 5.9, P=0.02) were both independent risk factors for EPE colonization.

ESBL-E: extended spectrum beta-lactamase producing Enterobacterales (which includes Enterobacteriaceae); CPO: carbapenemase producing organisms; CPE: carbapenemase producing Enterobacterales (which includes Enterobacteriaceae); CRE: carbapenem-resistant Enterobacterales (which includes Enterobacteriaceae); CRAB: carbapenem-resistant *Acinetobacter baumannii*; CRPA: carbapenem-resistant *Pseudomonas aeruginosa*; MDRAb: multidrug-resistant *A. baumannii*; XDRAb: extensively drug-resistant *A. baumannii*; IRAB: imipenem-resistant *Acinetobacter baumannii*; 3GCRE: third generation cephalosporin resistant enterobacterales; pAmp C-E: pAmp C-producing Enterobacterales; CRKP: Carbapenem-resistant *Klebsiella pneumoniae*; CIPR-E: ciprofloxacin-resistant Enterobacteriaceae; MDRO:multidrug-resistant organisms; MDRPA = multidrug-resistant *Pseudomonas aeruginosa*; AMR: antimicrobial resistance, NGS; next-generation sequencing

Conclusion

Duration of colonisation

All the systematic reviews and primary studies found that the colonisation rate decreases over time both in persons in the community, returning travellers, and patients in hospitals. However, persons in the community and healthy travellers had an overall lower risk for persistent colonisation and have a faster decolonisation compared to hospital patients. Loss of carrier state decreases exponentially the first 3 months in many studies before stabilising after 6 months. A considerable number of patients carry multidrug-resistant Enterobacterales after a year of follow up and few studies follow patients beyond 12 months. Some studies also showed differences in duration of colonisation between different lineages of ESBL-producing *E. coli*.

It is difficult to compare studies due to the heterogeneity; the study design of the included studies is different and there are variations in the follow-up period, sampling frequencies, loss to follow-up and definitions for clearance. The number of negative samples required for 'clearance' were in many studies only one negative sample.

Further studies are needed to examine duration of colonisation in different settings and with similar definitions of clearance and consistent sampling frequencies and follow-up periods.

Risk of transmission

There were few systematic reviews reporting on risk of transmission of multidrug-resistant Gram-negative bacteria. We only found studies reporting on transmission from colonised mother to their infants and transmission in households. The systematic review investigating transmission from colonised mother to their infants found a transmission rate around 30%.

The studies on transmission to household contacts showed a lower transmission from returned travellers to household contacts compared to transmission from discharged hospital patients to household contacts. One systematic review studying household transmission from index travellers found positive household contacts, but they carried different ESBL-producing *E. coli* strains than the respective travellers.

Further studies are needed investigating transmission rates in different settings.

Prevalence of colonisation in different patient populations and settings

The systematic reviews showed significant variation in prevalence, particularly high outside the Nordic region, notably in Southeast Asia, Africa, and parts of Southern and Eastern Europe. Studies specifically on asylum seekers and refugees in the Nordic countries and the Netherlands reported multidrug-resistant bacteria colonisation rates between 20-45%, with ESBL-E being the most common. Studies on patients hospitalised abroad found high colonisation rate of MDR, especially from transfers from southern and Western Asia. ICU treatment, short time since hospitalisation and antibiotic use were identified as predisposing factors.

Associated factors

Hospitalisation, and especially prolonged hospitalisation and ICU stays, as well as prior antibiotic use were associated with ESBL/CPO colonisation among hospitalised patients. Other associated factors were mechanical ventilation, surgery and use of central venous catheters. For residents of long-term care facilities, the same factors were identified, as well as previous colonisation or infection, urinary tract infections, and urinary catheter usage with ESBL-colonisation.

Reviews focusing on international travellers found that ESBL-E/CPE were likely to have been mostly acquired from Asia, Northern Africa, Sub-Saharan Africa, and Central and South America. A higher odds of detecting multidrug-resistant bacterial isolates was observed in medical travellers.

Colonisation was more often seen in travellers who'd received antibiotics during travel or had traveller's diarrhoea. Backpacker travellers more often had multidrug-resistant Enterobacterales. Primary studies from Nordic countries and the Netherlands found highest rates of ESBL-E colonisation among travellers returning from Asia and Northern Africa. Patients hospitalized or who underwent major invasive procedure in Eastern Europe displayed the highest rates of ESBL-E colonisation.

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99. van Dulm E, Tholen Aletta TR, Pettersson A, van Rooijen Martijn S, Willemsen I, Molenaar P, et al. High prevalence of multidrug resistant Enterobacteriaceae among residents of long term care facilities in Amsterdam, the Netherlands. *PloS one*. 2019;14(9):e0222200.
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101. van den Bunt G, Liakopoulos A, Mevius DJ, Geurts Y, Fluit AC, Bonten MJM, et al. ESBL/AmpC-producing Enterobacteriaceae in households with children of preschool age: prevalence, risk factors and co-carriage. *The Journal of antimicrobial chemotherapy*. 2017;72(2):589-95.

Appendices

Search strategies ESBL and CPO - colonisation

Contact person: Mari Molvik

Search: Ragnhild Agathe Ternes

Peer review: Bente Foss

Duplicate control in EndNote: Before duplicate control: 3476, 896 systematic reviews
After duplicate control: 2234, 437 systematic reviews

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions <1946 to September 19, 2024>

Date: 23.09.24

Number of hits: 1854 primary studies, 233 systematic reviews

1	beta-Lactamases/ or Cephalosporinase/ or ((beta adj (lactamase? or lactamhydrolase)) or betalactamase? or cephalosporinase or cephalixin amidase or beta lactam hydrolase or cefinase or ceftazidimase).tw,kf.	44792
2	ESBL.tw,kf.	11593
3	(carbapenemase? or CPE or CPO or CRE or CRAB or CRPA).tw,kf.	60449
4	((resistan* or "non-susceptibilit*" or nonsusceptibilit*) adj3 (acantex or alphacef or anticepim or axepim or axepime or axone or bacteripime or benaxona or biotrakson or biotriax or bioxon or "bmy 28142" or bmy28142 or broadced or brospec or "cef-3" or cefaflox or cefalogen or cefatriaxone or cefaxona or cefaxone or cefepim or cefepima or cefepime or cefepitax or ceficad or cefin or cefotal or cefotaksim or cefotaksime or cefotaxime or cefotaxime or cefotriaxon or cefotriaxone or cefriex or Ceftazidime or ceftrex or Ceftriakson or ceftrian or Ceftriaxone or ceftrilem or cefxon or "cephalosporanic acid?" or Cephalosporin? or cephin or cephtriaxone or cepim or cepimax or cepimex or cerixon or cikedrix or critipeme or deltacef or ecotrixon or elpicef or eurocef or exempla or ferfacef or forgram or fortaz or fortum or "forzyn beta" or gencef or glicocef or gomcephin or grifotriaxona or incephin or keftriaxon or kepatrix or loplatin or lyceft or maxcef or maxfrom or maxinject or maxipime or medoxonum or meqion or mesporin or monocef or nakaxone or "nb 8947" or nb8947 or novosef or oframax or pantrixon or pimaxef or quadrocef or retrokor or rinxofay or "ro 13 9904" or "rocefalin roche" or rocefin or rocephalin or rocephin or rocephine or rowecef or roxcef or roxon or salapime or samixon or sintrex or socef or "sp 1001" or sp1001 or sunflow or tacex or tazidime or "torocef-1" or trexofin or triaken or triax or triaxone or tricefin or	7865

	tricephin or trijec or verapime or xtenda or zefaxone or zefipime or "zefone 250").tw,kf.	
5	((resistan* or "non-susceptibilit*" or nonsusceptibility*) adj3 (doripenem or ertapenem or imipenem or meropenem or thienamycin*)).tw,kf.	3802
6	or/1-5	103693
7	(colonis* or coloniz* or carri* or screen*).tw,kf.	2163712
8	6 and 7	16730
9	(comment or editorial or letter).pt.	2283185
10	8 not 9	16566
11	limit 10 to yr="2014 -Current"	11290
12	limit 11 to "reviews (maximizes specificity)"	226
13	Meta-Analysis/ or Network Meta-Analysis/ or ((systematic* adj2 review*) or metaanal* or "meta anal*" or (review and ((structured or database* or systematic*) adj2 search*)) or "integrative review*" or (evidence adj2 review*)).tw,kf,bt.	588909
14	12 or (11 and 13)	253
15	limit 14 to (danish or english or german or norwegian or swedish) [systematiske oversikter med årtal- og språkavgrensing]	233
16	11 not 14	11037
17	exp "Scandinavian and Nordic Countries"/ or "Scandinavians and Nordic People"/ or Netherlands/	301124
18	(Scandinavi* or nordic or Norway or norwegian? or Norge or Svalbard or Spitsbergen or Jan Mayen or Sweden or swedish or swede? or Sverige or Denmark or danish or Danmark or Finland or finnish or finns or Åland or Aaland or alandi* or aalandi* or Suomi or Iceland or icelandic* or icelander* or "Fa?roe Islands" or fa?roes* or Greenland or Kalaallit Nunaat or Netherland* or Holland or Dutch).tw,cp,in,lg,kf,pl.	4171374
19	(sykehus* or sjukehus* or ((universitet* or University or univ) adj3 (haukeland or nordnorge or norge* or bergen or stavanger or tromsø or tromsøe or trondheim or levanger or gjovik or gjøvik or harstad or lillehammer or narvik or nesna or stord or haugesund or voldal or aalesund or alesund)) or ((universitet* or University or univ) adj1 nord) or sentralsjukehus* or sentralsykehus* or Finnmarkssykehuset or Helgelandssykehuset or Nordlandssykehuset or innlandet or "Olav? Hospital?" or revmatismesykehus or lungesykehus or "Hospitalet Betanien" or Kysthospitalet or Aleris or Feiringklinikken or Glittreklinikken or "Hjertesenteret i Oslo" or "Medi 3" or "Volvat Medisinske Senter" or "Helse Vest" or "Helse Stavanger" or "Helse fonna" or "helse bergen" or "helse forde" or "helse foerde" or sjukehusapotek* or sykehusapotek* or "helse midt norge" or "helse midtnorge" or "Ambulanse Midtnorge" or "Ambulanse Midt norge" or "helse nord" or "Helse Sorost" or "Helse Sor ost" or "Helse Soeroest" or "Helse Soer oest" or sunnaas or sunnas or sorlandet or soerlandet).in,tw,kf,pl.	63955
20	(Akershus or Viken or Austagder or Agder or Buskerud or Finnmark or Hedmark or Hordaland or Romsdal or Nordland or Nordtrondelag or Trondelag or Nordtroendelag or Troendelag or Oppland or Oslo or Rogaland or Fjordane or Sortrondelag or Soertroendelag or Telemark or	107112

	Troms or Vestagder or Vestfold or Ostfold or Oestfold or Longyearbyen or innlandet or vestland).in,tw,kf,pl.	
21	(sjukhus* or centralsjukhus* or laenssjukhus* or lanssjukhus* or lamsdelssjukhus* or laensdelssjukhus* or barnsjukhus* or ungdomssjukhus* or lasarett* or Regionsjukhus* or Narsjukhus* or Naersjukhus* or Specialistsjukhus* or Beckombergasykehuset or "Danvikens hospital" or Konradsberg or "karolinska institute?" or (karolinska adj2 hosp*) or ("astrid lindgren" adj2 hosp*) or sahlgrenska or Radiumhemmet or Sophiahemmet or Sodersjukhuset or Soedersjukhuset or Blekingesjukhuset or Anestesiklinik* or Linneuniversitetet or Mittuniversitetet or "Royal Institute of Technology" or ((Universitet* or universit* or univ) adj2 (norrland* or skaane? or skane? or lindkoping or orebro or lindkoeping or oerebro or lund or lunds or uppsala or gothenborg? or gothenburg? or goteborg? or goteburg? or goethenborg? or goethenborg? or goeteborg? or goeteborg? or umeaa? or umea? or luleaa or lulea or karlstad? or vaxjo or vaexjo or vaxjoe or vaexjoe or kalmar or tekniska or Linnaeus or Chalmers or malmo or malmoe or Malardalen? or Maelardalen? or karolinska))).in,tw,kf,pl.	343118
22	(Blekinge or dalarna? or gotland or gavleborg? or gaevleborg? or halland or jamtland* or jaemtland* or jonkoping? or joenkoping? or kalmar? or kronoberg? or norbotten or skaane or skane or stockholm? or sodermanland? or soedermanland? or uppsala? or varmland? or vaermland? or vasterbotten? or vaesterbotten? or vasternorrland? or vaesternorrland? or vastmanland? or vaestmanland? or gotaland? or orebro? or "oster gotland?" or goetaland? or oerebro? or "oester gotland?").in,tw,kf,pl.	253079
23	(sygehus* or ((Universitet* or universit* or hospital* or hosp) adj3 (amager* or Augustenborg* or Bornholm* or farso* or give or herning* or hobro* or koge or koege or orange* or randers or ringsted* or skagen* or "sct. hans*" or tarm or tonder* or toender* or thisted* or vejle* or viborg* or Aalborg* or aarhus* or Alborg* or arhus*)) or Specialhospital* or Universitetshospital* or Regionshospital* or "Psykiatrisk Cent*" or "Psykiaterapeutisk Cent*" or Psykiatricenter* or Kommunehospital* or Centralsygeh* or "Hammel Neurocenter*" or "Vest Ribe*" or Aabenraa* or Abenra* or Aroskobing* or Aroskobing* or Aeroeskobing* or Aroskobing* or allerup* or Bispebjerg* or Bronderslev* or Broenderslev* or copenhagen* or Esbjerg* or Fakse or Fredericia* or Frederiksberg* or frederikshavn* or Gentofte* or Glostrup* or Grenaa* or Grena* or Grindsted* or Haderslev* or Herlev* or Hjoerring* or Hjoerring* or holbaek* or Holbak* or Holstebro* or Horsens* or hovedstaden* or Hvidovre* or Kalundborg* or kobenhavn* or koebenhavn* or Kolding* or Korsor* or Korsoer* or Lemvig* or Middelfart* or Midtjylland* or Naestved* or Nakskov* or Nastved* or Nordjylland* or Nordsjaelland* or Nordsjalland* or Nykobing* or Nykobing* or Odense* or Poppelhus* or Rigshospitalet* or Ringkobing* or Ringkobing* or Risskov* or Roskilde* or Silkeborg* or Sjaelland* or Sjalland* or Skanderborg* or Skejby* or Slagelse* or Sonderborg* or Soenderborg* or Stolpegaard* or Svendborg* or Syddanmark* or sydvestjysk* or Syddansk* or "Tekniske Universitet*" or "IT	272558

	Universitetet*" or ITUniversitetet* or "aarhus univ*" or "aalborg univ*" or "U of Aarhus*" or "U of aalborg*" or "Univ of Aarhus*" or "Univ of aalborg*" or "arhus univ*" or "alborg univ*" or "U of Arhus*" or "U of alborg*" or "Univ of Arhus*" or "Univ of alborg*").tw,in,kf,pl.	
24	(tidsskrift for den norske lægeforening or Norsk Epidemiologi or lakartidningen or ugeskrift for læger).jn.	111018
25	or/17-24	4205700
26	16 and 25	1854

Database: Embase <1974 to 2024 September 20>
Date: 23.09.24
Number of hits: 736 primary studies, 215 systematic reviews

1	beta lactamase/ or Cephalosporinase/ or ((beta adj (lactamase? or lactamhydrolase)) or betalactamase? or cephalosporinase or cephaloxin amidase or beta lactam hydrolase or cefinase or ceftazidimase).tw,kf.	51607
2	extended spectrum beta lactamase/ or ESBL.tw,kf.	21649
3	carbapenemase/ or carbapenemase producing Enterobacteriaceae/ or (carbapenemase? or CPE or CPO or CRE or CRAB or CRPA).tw,kf.	87488
4	cephalosporin resistance/ or ceftazidime resistance/ or cefotaxime resistance/ or ((resistan* or "non-susceptibilit*" or nonsusceptibilit*) adj3 (acantex or alphacef or anticepim or axepim or axepime or axone or bacteripime or benaxona or biotrakson or biotriax or bioxon or "bmy 28142" or bmy28142 or broadced or brospec or "cef-3" or cefaflox or cefalogen or cefatriaxone or cefaxona or cefaxone or cefepim or cefepima or cefepime or cefepitax or ceficad or cefin or cefotal or cefotaksim or cefotaksime or cefotaxime or cefotaxime or cefotriaxon or cefotriaxone or cefriex or Ceftazidime or ceftrex or Ceftriakson or ceftrian or Ceftriaxone or ceftrilem or cefxon or "cephalosporanic acid?" or Cephalosporin? or cephin or cephtriaxone or cepim or cepimax or cepimex or cerixon or cikedrix or critipeme or deltacef or ecotrixon or elpicef or eurocef or exempla or ferfacef or forgram or fortaz or fortum or "forzyn beta" or gencef or glycocef or gomcephin or grifotriaxona or incephin or keftriaxon or kepatrix or loplatin or lyceft or maxcef or maxfrom or maxinject or maxipime or medoxonum or megiion or mesporin or monocef or nakaxone or "nb 8947" or nb8947 or novosef or oframax or pantrixon or pimaxef or quadrocef or retrokor or rinxofay or "ro 13 9904" or "rocefalin roche" or rocefin or rocephalin or rocephin or rocephine or rowecf or roxcef or roxon or salapime or samixon or sintrex or socef or "sp 1001" or sp1001 or sunflow or tacex or tazidime or "torocef-1" or trexofin or triaken or triax or triaxone or tricefin or tricephin or trijec or verapime or xtenda or zefaxone or zefipime or "zefone 250").tw,kf.	10842
5	((resistan* or "non-susceptibilit*" or nonsusceptibility*) adj3 (doripenem or ertapenem or imipenem or meropenem or thienamycin*)).tw,kf.	5475
6	or/1-5	144067
7	(colonis* or coloniz* or carri* or screen*).tw,kf.	2917033
8	6 and 7	22844
9	(Conference Abstract or Letter or Editorial).pt.	7405767
10	8 not 9	17869
11	limit 10 to yr="2014 -Current"	11914
12	limit 11 to "reviews (maximizes specificity)"	191
13	exp Meta-Analysis/ or "systematic review"/ or ((systematic* adj2 review*) or metaanal* or "meta anal*" or (review and ((structured or database* or	844296

	systematic*) adj2 search*)) or "integrative review*" or (evidence adj2 review*).tw,kf,bt.	
14	12 or (11 and 13)	246
15	limit 14 to (danish or english or german or norwegian or swedish)	244
16	limit 15 to embase	215
17	11 not 14	11668
18	exp scandinavia/ or exp north germanic people/ or Netherlands/	332440
19	(Scandnavi* or nordic or Norway or norwegian? or Norge or Svalbard or Spitsbergen or Jan Mayen or Sweden or swedish or swede? or Sverige or Denmark or danish or Danmark or Finland or finnish or finns or Åland or Åland or alandi* or aalandi* or Suomi or Iceland or icelandic* or icelander* or "Fa?roe Islands" or fa?roes* or Greenland or Kalaallit Nunaat or Netherland* or Holland).in,ad,tw,lg,kf.	2627145
20	(sykehus* or sjukehus* or ((universitet* or University or univ) adj3 (haukeland or nordnorge or norge* or bergen or stavanger or tromsø or tromsø or trondheim or levanger or gjovik or gjoevik or harstad or lillehammer or narvik or nesna or stord or haugesund or voldal or aalesund or alesund)) or ((universitet* or University or univ) adj1 nord) or sentralsjukehus* or sentralsykehus* or Finnmarkssykehuset or Helgelandssykehuset or Nordlandssykehuset or innlandet or "Olav? Hospital?" or revmatismesykehus or lungesykehus or "Hospitalet Betanien" or Kysthospitalet or Aleris or Feiringklinikken or Glittreklinikken or "Hjertesenteret i Oslo" or "Medi 3" or "Volvat Medisinske Senter" or "Helse Vest" or "Helse Stavanger" or "Helse fonna" or "helse bergen" or "helse forde" or "helse foerde" or sjukehusapotek* or sykehusapotek* or "helse midt norge" or "helse midtnorge" or "Ambulanse Midtnorge" or "Ambulanse Midt norge" or "helse nord" or "Helse Sorost" or "Helse Sor ost" or "Helse Soeroest" or "Helse Soer oest" or sunnaas or sunnas or sorlandet or soerlandet).in,ad,ti,ab,kf.	94412
21	(Akershus or Viken or Austagder or Agder or Buskerud or Finnmark or Hedmark or Hordaland or Romsdal or Nordland or Nordtrondelag or Trondelag or Nordtroendelag or Troendelag or Oppland or Oslo or Rogaland or Fjordane or Sortrondelag or Soertroendelag or Telemark or Troms or Vestagder or Vestfold or Ostfold or Oestfold or Longyearbyen or innlandet or vestland).in,ad,ti,ab,kf.	159676
22	(oslonorway or bergennorway or sandnesnorway or stavangernorway or trondheimnorway or tromsonorway or tromsønorway or Akershusnorway or Vikennorway or Austagdernorway or Agdernorway or Buskerudnorway or Finnmarknorway or Hedmarknorway or Hordalandnorway or Romsdالنorway or Nordlandnorway or Nordtrondelagnorway or Nordtroendelagnorway or Trondelagnorway or Troendelagnorway or Opplandnorway or Rogalandnorway or Fjordanenorway or Sortrondelagnorway or Sortroendelagnorway or Telemarknorway or Tromsnorway or Vestagdernorway or Vestfoldnorway or Ostfoldnorway or Oestfoldnorway or innlandetnorway or vestlandnorway).in,ad,ti,ab,kf.	753
23	(sjukhus* or centralsjukhus* or laenssjukhus* or lanssjukhus* or landsdelssjukhus* or laensdelssjukhus* or barnsjukhus* or ungdomssjukhus* or lasarett* or Regionsjukhus* or Narsjukhus* or Naersjukhus* or Specialistsjukhus* or Beckombergasykehuset or "Danvikens hospital" or Konradsberg or "karolinska institute?" or (karolinska adj2 hosp*) or ("astrid	493226

	lindgren" adj2 hosp*) or sahlgrenska or Radiumhemmet or Sophiahemmet or Sodersjukhuset or Soedersjukhuset or Blekingesjukhuset or Anestesiklinik* or Linneuniversitetet or Mittuniversitetet or "Royal Institute of Technology" or ((Universitet* or universit* or univ) adj2 (norrland* or skaane? or skane? or lindkoping or orebro or lindkoeping or oerebro or lund or lunds or uppsala or gothenborg? or gothenburg? or goteborg? or goteburg? or goethenborg? or goethenborg? or goeteborg? or goeteborg? or umeaa? or umea? or luleaa or lulea or karlstad? or vaxjo or vaexjo or vaxjoe or vaexjoe or kalmar or tekniska or Linnaeus or Chalmers or malmo or malmoe or Malardalen? or Maelardalen? or karolinska))).in,ad,ti,ab,kf.	
24	(Blekinge or dalarna? or gotland or gavleborg? or gaeleborg? or halland or jamtland* or jaemtland* or jonkoping? or joenkoping? or kalmar? or kronoberg? or norbotten or skaane or skane or stockholm? or sodermanland? or soedermanland? or uppsala? or varmland? or vaerland? or vasterbotten? or vaesterbotten? or vasternorrland? or vaesternorrland? or vastmanland? or vaestmanland? or gotaland? or orebro? or "oster gotland?" or goetaland? or oerebro? or "oester gotland?").in,ad,ti,ab,kf.	375951
25	(norrandsweden or skaanesweden or skanesweden or lindkopingsweden or lindkoepingsweden or orebrosweden or oerebrosweden or lundsweden or uppsalaweden or gothenborgsweden or gothenburgsweden or goteborgsweden or goteburgsweden or goethenborgsweden or goethenborgsweden or goeteborgsweden or goeteborgsweden or umeaasweden or umeasweden or luleaasweden or luleasweden or karlstadsweden or vaxjosweden or vaexjosweden or vaxjoesweden or vaexjoesweden or kalmarsweden or malmosweden or malmoesweden or Malardalensweden or Maelardalensweden or Blekingesweden or dalarnasweden or gotlandsweden or gavleborgsweden or gaeleborgsweden or hallandsweden or jamtlandsweden or jaemtlandsweden or jonkopingsweden or joenkopingsweden or kalmarsweden or kronobergsweden or norbottensweden or stockholmsweden or sodermanlandsweden or soedermanlandsweden or uppsalaweden or varmlandsweden or vaerlandsweden or vasterbottensweden or vaesterbottensweden or vasternorrandsweden or vaesternorrandsweden or vastmanlandsweden or vaestmanlandsweden or gotalandsweden or goetalandsweden or orebrosweden or oerebrosweden or gotlandsweden or Vasteraassweden or Vaesterassweden or helsingborgsweden or norrkopingsweden or norrkoepingsweden).in,ad,ti,ab,kf.	2140
26	(sygehus* or ((Universitet* or universit* or hospital* or hosp) adj3 (amager* or Augustenborg* or Bornholm* or farso* or give or herning* or hobro* or koge or koege or oringe* or randers or ringsted* or skagen* or "sct. hans*" or tarm or tonder* or toender* or thisted* or vejle* or viborg* or Aalborg* or aarhus* or Alborg* or arhus*)) or Specialhospital* or Universitetshospital* or Regionshospital* or "Psykiatrisk Cent*" or "Psykoaterapeutisk Cent*" or Psykiatricenter* or Kommunehospital* or Centralsygeh* or "Hammel Neurocenter*" or "Vest Ribe*" or Aabenraa* or Abenra* or Aeroskobing* or Aroskobing* or Aeroeskobing* or Aroskobing* or allerup* or Bispebjerg* or Bronderslev* or Broenderslev* or copenhagen* or Esbjerg* or Fakse or Fredericia* or Frederiksberg* or frederikshavn* or Gentofte* or Glostrup* or Grenaa* or Grena* or Grindsted* or Haderslev* or Herlev* or Hjoerring* or Hjoerring* or holbaek* or Holbak* or Holstebro* or Horsens* or hovedstaden*	405616

	or Hvidovre* or Kalundborg* or kbenhavn* or koebenhavn* or Kolding* or Korsor* or Korsoer* or Lemvig* or Middelfart* or Midtjylland* or Naestved* or Nakskov* or Nastved* or Nordjylland* or Nordsjaelland* or Nordsjælland* or Nykobing* or Nykoebing* or Odense* or Poppelhus* or Rigshospitalet* or Ringkobing* or Ringkoebing* or Risskov* or Roskilde* or Silkeborg* or Sjaelland* or Sjælland* or Skanderborg* or Skejby* or Slagelse* or Sonderborg* or Soenderborg* or Stolpegaard* or Svendborg* or Syddanmark* or sydvestjysk* or Syddansk* or "Tekniske Universitet*" or "IT Universitetet*" or ITUniversitetet* or "aarhus univ*" or "aalborg univ*" or "U of Aarhus*" or "U of aalborg*" or "Univ of Aarhus*" or "Univ of aalborg*" or "arhus univ*" or "alborg univ*" or "U of Arhus*" or "U of alborg*" or "Univ of Arhus*" or "Univ of alborg*").in,ad,ti,ab,kf.	
27	(amagerdenmark or Augustenborgdenmark or Bornholmdenmark or farsodenmark or farsoedenmark or givedenmark or herningdenmark or hobrodenmark or kogedenmark or koegedenmark or oringedenmark or randersdanmark or ringsteddenmark or tarmdenmark or thisteddenmark or tonderdenmark or toenderdenmark or Vejledanmark or viborgdenmark or Aalborgdenmark or aarhusdenmark or Alborgdenmark or arhusdenmark).in,ad,ti,ab,kf.	333
28	(tidsskrift for den norske laegeforening or tidsskrift for den norske laegeforening tidsskrift for praktisk or tidsskrift for den norske laegeforening tidsskrift for praktisk medicin ny raeke or Norsk Epidemiologi or lakartidningen or ugeskrift for laeger).jn.	94948
29	or/18-28	2685991
30	17 and 29	845
31	limit 30 to embase	736

Database: Cochrane Central Register of Controlled Trials

Issue 8 of 12, August 2024

Cochrane Database of Systematic Reviews

Issue 9 of 12, September 2024

Date: 23.09.24

Number of hits: 22 trials, 2 systematic reviews

#1	[mh ^"beta-Lactamases"] or [mh ^Cephalosporinase] or ((beta NEXT (lactamase? or lactamhydrolase)) or betalactamase? or cephalosporinase or "cephalexin amidase" or "beta lactam hydrolase" or cefinase or ceftazidimase):ti,ab	653
#2	ESBL:ti,ab	291
#3	(carbapenemase? or CPE or CPO or CRE or CRAB or CRPA):ti,ab	1497
#4	((resistan* or "non-susceptibility" or "non-susceptibilities" or nonsusceptibility or nonsusceptibilities) NEAR/3 (acantex or alphacef or anticepim or axepim or axepime or axone or bacteripime or benaxona or biotrakson or biotriax or bioxon or "bmy 28142" or bmy28142 or broadced or brospec or "cef-3" or cefaflox or cefalogen or cefatriaxone or cefaxona or cefaxone or cefepim or cefepima or cefepime or cefepitax or ceficad or cefin or cefotal or cefotaksim or cefotaksime or cefotaxime or cefotaxime or cefotriaxon or cefotriaxone or cefriex or Ceftazidime or ceftrex or Ceftriakson or ceftrian or Ceftriaxone or ceftirlem or cefxon or "cephalosporanic acid" or "cephalosporanic acids" or Cephalosporin? or cephin or cephtriaxone or cepim or cepimax or cepimex or cerixon or cikedrix or critipeme or deltacef or ecotrixon or elpicef or eurocef or exempla or ferfacef or forgram or fortaz or fortum or "forzyn beta" or gencef or glicocef or gomcephin or grifotriaxona or incephin or keftriaxon or keptrix or loplatin or lyceft or maxcef or maxfrom or maxinject or maxipime or medoxonum or megiom or mesporin or monocef or nakaxone or "nb 8947" or nb8947 or novosef or oframax or pantrixon or pimaxef or quadrocef or retrokor or rinxofay or "ro 13 9904" or "rocefalin roche" or rocefim or rocephalin or rocephin or rocephine or rowceft or roxcef or roxon or salapime or samixon or sintrex or socef or "sp 1001" or sp1001 or sunflow or tacex or tazidime or "torocef-1" or trexofin or triaken or triax or triaxone or tricefin or tricephin or trijec or verapime or xtenda or zefaxone or zefipime or "zefone 250"):ti,ab	167
#5	((resistan* or "non-susceptibility" or "non-susceptibilities" or nonsusceptibility or nonsusceptibilities) NEAR/3 (doripenem or ertapenem or imipenem or meropenem or thienamycin*)):ti,ab	56
#6	{or #1-#5}	2381
#7	(colonis* or coloniz* or carri* or screen*):ti,ab	168349
#8	#6 and #7	407
#9	#8 with Cochrane Library publication date Between Jan 2014 and Sep 2024, in Cochrane Reviews	2

#10	[mh "Scandinavian and Nordic Countries"] or [mh ^"Scandinavians and Nordic People"] or [mh Netherlands] or (Scandinavi* or nordic or Norway or norwegian? or Norge or Svalbard or Spitsbergen or "Jan Mayen" or Sweden or swedish or swede? or Sverige or Denmark or danish or Danmark or Finland or finnish or finns or Aland or Aaland or alandi* or aalandi* or Suomi or Iceland or icelandic* or icelander* or "Faroe Islands" or "Faeroe Islands" or fa?roes* or Greenland or "Kalaallit Nunaat" or Netherland* or Holland or Dutch):ti,ab	46022
#11	#8 and #10	24
#12	#11 with Cochrane Library publication date Between Jan 2014 and Sep 2024, in Trials	22
#13	#11 with Publication Year from 2014 to 2024, in Trials	21
#14	#12 or #13	22

Database: Web of Science Core Collection

- WOS.SCI: 1987 to 2024

- WOS.AHCI: 1987 to 2024

- WOS.ESCI: 2018 to 2024

- WOS.SSCI: 1987 to 2024

Date: 23.09.24

Number of hits: 884 primary studies, 250 systematic reviews

14	#13 AND (CU==("NORWAY" OR "SWEDEN" OR "DENMARK" OR "FINLAND" OR "ICELAND" OR "NETHERLANDS"))	 Exact search	884
13	#9 not #11	 Exact search	12,822
12	#11 and Spanish or French (Exclude – Languages)	 Exact search	250
11	#9 AND #10	 Exact search	253
10	TS=(("systematic*" NEAR/1 "review*") or ("review" and (("structured" or "database*" or "systematic*") NEAR/1 "search*")) or "integrative review*" or ("evidence" NEAR/1 "review*")) OR TI=("metaanal*" or "meta anal*") OR AB=("metaanal*" or "meta anal*")	 Exact search	667,039
9	#8 Index Date 2014-01-01 to 2024-09-20	 Exact search	13,075
8	#6 AND #7	 Exact search	19,697
7	TS=(colonis* or coloniz* or carri* or screen*)	 Exact search	3,601,286
6	#1 OR #2 OR #3 OR #4 OR #5	 Exact	135,943

		search	
5	TS=((resistan* or "non-susceptibilit*" or nonsusceptibilit* or nonsusceptibilit*) NEAR/2 (doripenem or ertapenem or imipenem or meropenem or thienamycin*))	 Exact search	3,860
4	TS=((resistan* or "non-susceptibilit*" or nonsusceptibilit* or nonsusceptibilit*) NEAR/2 (acantex or alphacef or anticepim or axepim or axepime or axone or bacteripime or benaxona or biotrakson or biotriax or bioxon or "bmy 28142" or bmy28142 or broadced or brospec or "cef-3" or cefaflox or cefalogen or cefatriaxone or cefaxona or cefaxone or cefepim or cefepima or cefepime or cefepitax or ceficad or cefin or cefotal or cefotaksim or cefotaksime or cefotaxime or cefotaxime or cefotriaxon or cefotriaxone or cefriex or Ceftazidime or ceftrex or Ceftriaxon or ceftrian or Ceftriaxone or ceftrilem or cefxon or "cephalosporanic acid" or "cephalosporanic acids" or Cephalosporin\$ or cephin or cephtriaxone or cepim or cepimax or cepimex or cerixon or cikedrix or critipeme or deltacef or ecotrixon or elpicef or eurocef or exempla or ferfacef or forgram or fortaz or fortum or "forzyn beta" or gencef or glicocef or gomcephin or grifotriaxona or incephin or keftriaxon or kepatrix or loplatin or lyceft or maxcef or maxfrom or maxinject or maxipime or medoxonum or megion or mesporin or monocef or nakaxone or "nb 8947" or nb8947 or novosef or oframax or pantrixon or pimaxef or quadrocef or retrokor or rinxofay or "ro 13 9904" or "rocefalin roche" or rocefin or rocephalin or rocephin or rocephine or rowecef or roxcef or roxon or salapime or samixon or sintrex or socef or "sp 1001" or sp1001 or sunflow or tacex or tazidime or "torocef-1" or trexofin or triaken or triax or triaxone or tricefin or tricephin or trijec or verapime or xtenda or zefaxone or zefipime or "zefone 250"))	 Exact search	7,487
3	TS=(carbapenemase\$ or CPE or CPO or CRE or CRAB or CRPA)	 Exact search	94,565
2	TS= ESBL	 Exact search	11,837
1	TS=((beta NEAR/0 (lactamase\$ or lactamhydrolase)) or betalactamase\$ or cephalosporinase or "cephalexin amidase" or "beta lactam hydrolase" or cefinase or ceftazidimase)	 Exact search	42,103

Database: Epistemonikos

Date: 23.09.24

Number of hits: 227 systematic reviews/broad synthesis

Note: Simplified search strategy due to the limited search functionality

((("beta lactamase" or "beta lactamases" or betalactamase* or cephalosporinase or "cephalexin amidase" or "beta lactam hydrolase" or cefinase or ceftazidimase or ESBL or carbapenemase or carbapenemases or CPE or CPO or CRE or CRAB or CRPA) AND (colonis* or coloniz* or carri* or screen*)))

Publication year range From: 2014 To: 2024

Publication type: Systematic review (131 hits), Broad synthesis (6 hits)

((resistan* or "non-susceptibility" or "non-susceptibilities" or nonsusceptibility or nonsusceptibilities) AND (acantex or alphacef or anticepim or axepim or axepime or axone or bacteripime or benaxona or biotrakson or biotriax or bioxon or "bmy 28142" or bmy28142 or broadced or brospec or "cef-3" or cefaflox or cefalogen or cefatriaxone or cefaxona or cefaxone or cefepim or cefepima or cefepime or cefepitax or ceficad or cefin or cefotal or cefotaksim or cefotaksime or cefotaxime or cefotaxime or cefotriaxon or cefotriaxone or cefriex or Ceftazidime or ceftrex or Ceftriakson or ceftrian or Ceftriaxone or ceftrilem or cefxon or "cephalosporanic acid" or "cephalosporanic acids" or Cephalosporin or Cephalosporins or cephin or cephtriaxone or cepim or cepimax or cepimex or cerixon or cikedrix or critipeme or deltacef or ecotrixon or elpicef or eurocef or exempla or ferfacef or forgram or fortaz or fortum or "forzyn beta" or gencef or glicocef or gomcephin or grifotriaxona or incephin or keftriaxon or keprix or loplatin or lyceft or maxcef or maxfrom or maxinject or maxipime or medoxonum or megion or mesporin or monocef or nakaxone or "nb 8947" or nb8947 or novosef or oframax or pantrixon or pimaxef or quadrocef or retrokor or rinxofay or "ro 13 9904" or "rocefallin roche" or rocefin or rocephalin or rocephin or rocephine or rowcef or roxcef or roxon or salapime or samixon or sintrex or socef or "sp 1001" or sp1001 or sunflow or tacex or tazidime or "torocef-1" or trexofin or triaken or triax or triaxone or tricefin or tricephin or trijec or verapime or xtenda or zefaxone or zefipime or "zefone 250") AND (colonis* or coloniz* or carri* or screen*)))

Publication year range From: 2014 To: 2024

Publication type: Systematic review (69 hits), Broad synthesis (3 hits)

((resistan* or "non-susceptibility" or "non-susceptibilities" or nonsusceptibility or nonsusceptibilities) AND (doripenem or ertapenem or imipenem or meropenem or thienamycin*) AND (colonis* or coloniz* or carri* or screen*)))

Publication year range From: 2014 To: 2024

Publication type: Systematic review (17 hits), Broad synthesis (1 hit)

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