Synopsis (250 words maximum),

Introduction

Materials and methods

PubMed and Scopus were searched in all fields using the search terms (((ESBL) OR Extended-spectrum beta-lactamase)) AND (((Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cameroon OR Cape Verde OR Central African Republic OR Chad OR Comoros OR Republic of the Congo OR Congo Brazzaville OR Democratic republic of the Congo OR Cote d'Ivoire OR Djibouti OR Equatorial Guinea OR Eritrea OR Ethiopia OR Gabon OR The Gambia OR Ghana OR Guinea OR Guinea-Bissau OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mozambique OR Namibia OR Niger OR Nigeria OR Reunion OR Rwanda OR Sao Tome and Principe OR Senegal OR Seychelles OR Sierra Leone OR Somalia OR South Africa OR Sudan OR Swaziland OR Eswatini OR Tanzania OR Togo OR Uganda OR Western Sahara OR Zambia OR Zimbabwe) OR Africa)). Abstracts were extracted into Endnote X7.8 (Thomson Reuters, United States) and independently reviewed against inclusion criteria by two authors (JL and RL), with disagreements settles by consensus. Inclusion criteria were any cross-sectional or study that had screened for gut mucosal carriage of ESBL-E in any population in sub-Saharan Africa for which it was possible to extract a numerator and denominator to calculate an ESBL-E carriage prevalence. Studies were excluded if it the sampled population was not clearly defined (i.e. laboratory based studies), or if the laboratory techniques aimed to isolate only a particular organism or type of organism (e.g. Enteropathogenic *E. coli).*

Full-text review of included studies was then undertaken, with studies assessed against the same inclusion criteria, again with disagreements settles by consensus. Data were then extracted into a Microsoft Excel spreadsheet (Microsoft, United States): study title and authors, year of publication, dates of sample collection, inclusion criteria, median age or participants. Details of microbiologic testing procedures, number of participants and number of participants from whom ESBL-E were isolated, and any risk factors for ESBL-E that were assessed and/or found to be associated with ESBL-E carriage. Data were extracted by two authors independently (RL and JL) and any inconsistencies corrected by re-review of the original paper. For cohort studies only the baseline prevalence was included. Prevalence was presented as forest plots with exact binomial confidence intervals; age group (neonate, child, adult, as per study definition) and location of sampling (community, outpatient, on hospital admission, hospital) were selected as a priori subgroups that we hypothesised may explain heterogeneity in ESBL-E prevalence, and analyses were stratified by these subgroups. Pooled random effect summary estimates of prevalence, where calculated, were generated using the *metaprop* package in R using the inverse variance method with a logit transformation. All analysis was undertaken using R v3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

Risk of bias of included studies was assessed with ……

The protocol of this review was published on PROSPERO (PROSPERO ID CRD42019123559).

Results

Of 2975 identified unique studies, 32 were included in this review (Figure 1), from 19 countries in sSA (Table 1). Some countries were over-represented: studies from three countries – Tanzania (n=7), Madagascar (n=4) and Cameroon (n=4) together made up 15/32 (47%) of the available studies. In total, 8619 participants were included and for 7232/8619 (84%) it was possible to disaggregate the participants into age groups: 4313/7232 (60%) were adults, 2470/7232 (34%) children and 449/7232 (6%) neonates. 2302/8619 (27%) of included participants were community members, 1729/8619 (20%) were outpatients, 2836/8619 (33%) were sampled on admission to hospital, and 1534/8619 (18%) were inpatients. 6/32 studies were cohort studies; all of these studies followed patients up whilst hospitalised. No study longitudinally sampled community members or followed participants after they were discharged from hospital

The risk of bias was assessed as … Several studies recruited a selected group such as pregnant women, street children, or food handlers in schools and as such are likely to produce a biased estimate of community prevalence.



Figure 1: Flow chart of included studies.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Year Pub. | Study Period | Country | Study Type | Inclusion | Age group | Median age | n |
| Ruppe 2009 | 2009 | NR | Senegal | Cross sec. | Children in village selected for remoteness | Children | 6.9yr\* | 20 |
| Tande 2009 | 2009 | 2003 | Mali | Cross sec. | Orphanage children | Children | NR | 38 |
|  |  |  |  |  | Orphanage staff | Adults | NR | 30 |
| Andriatahina 2010 | 2010 | 2008 | Madagascar | Cohort | Inpatients | Children | 38.3m | 244 |
| Herindrainy 2011 | 2011 | 2009 | Madagascar | Cross sec. | Health centre attendees | Adults | NR | 306 |
|  |  |  |  |  | Health centre attendees | Children | NR | 147 |
| Woerther 2011 | 2011 | 2007-08 | Niger | Cohort | Children with SAM, inpatients | Children | 16.3m\* | 55 |
| Albrechtova 2012 | 2012 | 2009 | Kenya | Cross sec. | Community members | Adults | NR | 23 |
| Isendahl 2012 | 2012 | 2010 | Guinea-Bissau | Cross sec. | Children att. hospital w/ fever or tachycardia | Children | NR | 408 |
| Lonchel 2012 | 2012 | 2009 | Cameroon | Cross sec. | Students in the community | Adults | 24.7yr\* | 150 |
|  |  |  |  |  | Outpatients | Adults | 36.9yr\* | 208 |
| Lonchel 2013 | 2013 | 2009 | Cameroon | Cross sec. | Inpatients | Adults | 46.8yr\* | 121 |
| Magoue 2013 | 2013 | 2010 | Cameroon | Cross sec. | Hospital workers and their families | Adults | NR | 87 |
|  |  |  |  |  | Inpatients | Adults | NR | 208 |
|  |  |  |  |  | Relatives and carers of inpatients | Adults | NR | 63 |
|  |  |  |  |  | Outpatients | Adults | NR | 232 |
| Schaumburg 2013 | 2013 | 2010-11 | Gabon | Cross sec. | Hospital inpatients | Children | NR | 200 |
| Nelson 2014 | 2014 | 2013 | Tanzania | Cohort | Pregnant women and neonates, inpatient | Neonate | 0d | 126 |
|  |  |  |  |  |  | Adults | 26.5yr\* | 113 |
| Chereau 2015 | 2015 | 2013-14 | Madagascar | Cross sec. | Pregnant women in the community | Adults | 26yr\* | 356 |
| Desta 2016 | 2016 | 2012 | Ethiopia | Cross sec. | Inpatients | Adults | 35yr | 154 |
|  |  |  |  |  | Inpatients | Children | 7yr | 94 |
|  |  |  |  |  | Inpatients | Neonate | 9d | 19 |
| Djuikoue 2016 | 2016 | 2011-12 | Cameroon | Cross sec. | Outpatient women with susp. UTI | Adults | NR | 86 |
| Farra 2016 | 2016 | 2013 | CAR | Cross sec. | Healthy community controls from diarrhoea study | Children | 10.5m | 134 |
| Kurz 2016 | 2016 | 2014 | Rwanda | Cohort | Inpatients and one main caregiver | both | 29yr | 753 |
| Mshana 2016 | 2016 | 2014 | Tanzania | Cross sec. | Community members | both | 10yr | 334 |
| Ribeiro 2016 | 2016 | 2013 | Angola | Cross sec. | Community members no antibiotics/hospital exposure last 3 m | Adults | NR | 18 |
| Tellevik 2016 | 2016 | 2010-11 | Tanzania | Cross sec. | <2yr attending health centre for vaccine | Children | NR | 250 |
|  |  |  |  |  | Inpatients | Children | NR | 353 |
| Magwenzi 2017 | 2017 | 2015 | Zimbabwe | Cohort | Inpatient within 24hr of admission | Children | 1.0yr | 164 |
| Moremi 2017 | 2017 | 2015 | Tanzania | Cross sec. | Street children | Children | 14.2yr\* | 107 |
| Wilmore 2017 | 2017 | 2014-15 | Zimbabwe | Cross sec. | Outpatient, HIV infected, stable on ART | Children | 11yr | 175 |
| Chirindze 2018 | 2018 | 2016 | Mozambique | Cross sec. | Students in the community | Adults | NR | 275 |
| Founou 2018 | 2018 | 2017 | South Africa | Cohort | On hospital admission | Adults | NR | 43 |
| Herindrainy 2018 | 2018 | 2015-16 | Madagascar | Cross sec. | Pregnant women at delivery (home/facility) | Adults | 26yr\* | 275 |
| Katakweba 2018 | 2018 | 2011-13 | Tanzania | Cross sec. | Community members | Adults | NR | 70 |
| Marando 2018 | 2018 | 2016 | Tanzania | Cross sec. | Neonates with sepsis | Neonate | 6d | 304 |
| Moremi 2018 | 2018 | 2014-15 | Tanzania | Cohort | On hospital admission | Adults | NR | 930 |
| Nikema Pessinaba 2018 | 2018 | 2015-16 | Togo | Cross sec. | <5yr with febrile gastroenteritis | Children | NR | 81 |
| Sanneh 2018 | 2018 | 2015 | The Gambia | Cross sec. | Food handlers in schools | Adults | 37yr\* | 565 |
| Stanley 2018 | 2018 | 2017 | Uganda | Cross sec. | Participants who reared animals, attending health facility with a fever and/or diarrhea but without malaria | both | 21.7yr\* | 300 |

Table 1: Details of included studies. CAR = Central African Republic; ART = antiretroviral therapy; UTI = urinary tract infection; NR = not reported. yr = year; m = months, d = days, hr = hours. \* = mean rather than median

Overall ESBL carriage prevalence was extremely heterogeneous across studies ranging from 5-84% with no trend by year (supplementary figure S1). Some heterogeneity was explained by location of sampling (Figures 2 and 3): inpatients tended to have the highest carriage prevalence with community members the least and the other groups intermediate. There was no clear difference in prevalence between neonates, children or adults (Figures 2 and 3).



Figure 2: ESBL carriage by study stratified by location of sampling and age group. Adults are shown in blue, children in red, and neonates in green.



Figure 3: ESBL carriage by study with pooled random effect estimates stratified by location of sampling.

Discussion

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Transparency declarations

References.

Supplementary appendix



Supplementary figure S1: Overall ESBL-E colonization prevalence by study.