



HAL
open science

Current status of resistance to antibiotics in the Democratic Republic of the Congo: A review

David Lupande-Mwenebitu, Sophie Alexandra Baron, Larbi Zakaria Nabti, Octavie Lunguya-Metila, Jean-Philippe Lavigne, Jean-Marc Rolain, Seydina Mouhamadou Diene

► To cite this version:

David Lupande-Mwenebitu, Sophie Alexandra Baron, Larbi Zakaria Nabti, Octavie Lunguya-Metila, Jean-Philippe Lavigne, et al.. Current status of resistance to antibiotics in the Democratic Republic of the Congo: A review. *Journal of Global Antimicrobial Resistance*, 2020, 22, pp.818-825. 10.1016/j.jgar.2020.07.008 . hal-03149719

HAL Id: hal-03149719

<https://amu.hal.science/hal-03149719>

Submitted on 22 Aug 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

1 **Current status of resistance to antibiotics in Democratic Republic of Congo: a Review**

2 David Lupande-Mwenebitu^{1,2}, Sophie Alexandra Baron¹, Larbi Zakaria Nabti¹, Octavie

3 Lunguya-Metila³, Jean-Philippe Lavigne⁴, Jean-Marc Rolain^{1,5*}, Seydina M. Diene^{1,5*}

4

5 **1.** Aix Marseille Univ, IRD, APHM, MEPHI, Faculté de Pharmacie, 19-21 boulevard Jean
6 Moulin, 13385, Marseille CEDEX 05, France.

7 **2.** Université Catholique de Bukavu (UCB), Hôpital Provincial Général de Référence de
8 Bukavu, République Démocratique du Congo.

9 **3.** Cliniques Universitaires de Kinshasa, Service de Microbiologie, Kinshasa, République
10 Démocratique du Congo

11 **4.** VBMI, INSERM U1047, Université de Montpellier, Service de Microbiologie et Hygiène
12 hospitalière, CHU Nîmes, Nîmes, France

13 **5.** IHU Méditerranée Infection, 19-21 boulevard Jean Moulin, 13385, Marseille CEDEX 05,
14 France.

15 * **Corresponding authors :**

16 **Address :** Aix Marseille Univ, IRD, APHM, MEPHI, IHU Méditerranée Infection, Faculté de
17 Pharmacie, 19-21 boulevard Jean Moulin, 13385 Marseille CEDEX 05, France.

18 **Phone:** (33) 4 13 73 24 01

19 **Email-1:** seydina.diene@univ-amu.fr

20 **Email-2:** jean-marc.rolain@univ-amu.fr

21 **Keywords:** Antimicrobial resistance genes, Democratic Republic of Congo,

22 *Enterobacteriaceae*, Extended-spectrum β -lactamases, methicillin-resistant *Staphylococcus*

23 *aureus*.

24

25 **Abstract**

26 An overview of the literature was conducted to assess prevalence and mechanisms of
27 antibiotic resistance to date, mainly to β -lactam antibiotics, cephalosporins, carbapenems,
28 colistin and tigecycline in DR Congo. English and French publications were listed and
29 analysed using PubMed/Medline, Google Scholar and African Journals database between
30 January 1st, 1990 and December 31, 2019. For the 30 published articles found: i) Bacterial
31 resistance to antibiotics concerned both Gram-negative and Gram-positive bacteria; ii)
32 Multidrug resistance prevalence was the same in half of *Streptococcus pneumoniae* isolates;
33 iii) A worrying prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) was noted,
34 associated with co-resistance to several other antibiotics; iv) Resistance to 3rd generation
35 cephalosporins was very high in *Enterobacteriaceae*, mainly due to *bla*_{CTX-M-1} group and
36 *bla*_{SHV} genes. Data on carbapenem and colistin resistance were not available until now.
37 Further work is required to set up a surveillance system for antibiotic resistance in this
38 country.

39

40 **Introduction**

41 There is a growing concern on antimicrobial resistance (AMR) worldwide [1].
42 Resistance against antimicrobial agents in clinically relevant bacteria is one of the most
43 imminent threats to public health and especially to our most vulnerable patient populations
44 [2,3]. The treatment of bacterial infections in Africa is largely empirical and, in most
45 instances, there are no laboratory results to guide therapy [4,5]. The spread of AMR bacteria is
46 problematic for the medical community as a whole as it compromises empirical treatment
47 regimens by delaying the administration of appropriate antibiotic therapy and reducing
48 appropriate treatment options [6,7]. AMR remains a real challenge in resource-limited
49 countries due to a lack of available antibiotics with multidrug-resistant isolates being labelled
50 on the basis of a small number of antibiotics tested, with economic consequences and yet the
51 use of the old molecules is very effective. The consequences of AMR are not limited to
52 patients with infections, but to a whole system including the environmental and agro-pastoral
53 sector that hemming enough resistance genes. Hence, there is a need for action to significantly
54 reduce the expansion of the phenomenon, whose distribution varies considerably from one
55 country to another [8,9]. To combat the global threat of AMR, improved surveillance to detect
56 emerging and long-term resistance trends is vital, several global initiatives, such as the
57 Fleming Fund, have been recently established to improve laboratory capacity in low- and
58 middle-income countries [10].

59 As recently reported, there is a link between antibiotic resistance genes found in
60 human pathogens and those found in non-pathogenic, commensal and environmental
61 organisms, prompting further studies of natural and human-associated reservoirs of resistance
62 genes [11]. Many hypotheses can be evoked, even though the relationship between antibiotic
63 use and antibiotic resistance remains complex [12]. Resistance selection pressure continues as

64 antimicrobials are released into the environment, largely while remaining in their active
65 forms. These drugs frequently found in wastewater for example contributed greatly to the
66 environmental selection of antibiotic-resistant bacteria [13-17]. As reported by many health
67 care settings, *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*
68 have been identified as emerging organisms of concern for multidrug resistance, and have
69 encouraged researches in this area [18,19]. Resistance to antibiotics is the result of either by
70 reducing its affinity, lowering its concentration, or destroying it in order to effectively reduce
71 or cancel the interaction with its target [20]. Therefore, depending on the involved
72 mechanism, the resistance level can vary considerably [21].

73 Over the past decade, the increase in multidrug resistance of Gram-negative rods and
74 in particular the spread of resistance to carbapenems in *Enterobacteriaceae*, *Pseudomonas*
75 *spp.* and *Acinetobacter spp.*, has prompted the return of colistin (or polymyxin E) as a
76 treatment of last resort. Extended-spectrum β -lactamase (ESBL)-producing pathogens and
77 methicillin resistant *Staphylococcus aureus* (MRSA) are endemic in many hospitals
78 worldwide and are also increasingly detected in the community [22-25]. Carbapenem-resistant
79 enterobacterial infections (CRE) are being increasingly observed, mainly in health care
80 facilities, but also in the community; they are associated with management difficulties due to
81 the lack of alternative active molecules and cause outbreaks difficult to control in health care
82 facilities in low-income countries where hygiene is poor and the population is overcrowded,
83 in addition to an epidemic context of ESBL that was still not effectively controlled [26].

84

85 **Challenge of humanitarian disaster, infectious diseases and AMR spread in war context**

86 In Democratic Republic of Congo (DRC), data on AMR are scarce; some bacteria are
87 being included in surveillance cross sectional study, such as *Salmonella* spp. and *S. aureus*,
88 but there are unknown prospects focused on other bacteria and in many parts of the country
89 [27,28]. The DRC is a vast country (2.3 million km of area) divided into 26 provinces. Each
90 province is divided into health districts, which in turn are divided into health zones (called
91 “zones de santé”). A health zone in the DRC corresponds to what is internationally referred to
92 as a health district [29]. The conflict in DRC has resulted in a health-system collapse and
93 created a humanitarian disaster. An estimated 5.4 million excess deaths occurred from 1997 to
94 2004, with fewer than 10% attributable to violence and the rest to preventable and treatable
95 medical conditions, such as malaria, diarrhea, pneumonia, and malnutrition [30]. Armed
96 conflicts and other disastrous natural phenomena can lead to major population displacements.
97 An emergency unsustainable infrastructure is temporarily built, and often with overcrowding,
98 insufficient if not insufficient drinking water and sanitation, which gives its populations a risk
99 of exposure to communicable diseases, especially those with epidemic potential [31]. The
100 country had been the site of two wars involving multiple African nations and armed conflict
101 between rebels and soldiers for the past 16 years, characterized by extreme violence, massive
102 population displacements from east to west, and the collapse of all existing infrastructure
103 [32,33]. Massive population movements are at the root of most risk factors, people are
104 displaced to regions and areas where resources and services are insufficient and where contact
105 with other naïve populations with new vectors of infectious diseases is potentially more
106 frequent. This leads to large numbers of people going to camps, often associated with
107 overcrowding, inadequate housing and poor water conditions, resulting in the spread of
108 pathogenic microorganisms, as reported by UNHCR in January 2018 in Eastern Congo (**Fig.**
109 **1**) [34,35].

110 The deterioration of health services is probably one of the main risk factors for communicable
111 diseases in this type of humanitarian disaster, both for individuals and populations. Access to
112 health care in such conditions is impossible, which is a key risk factor for the serious
113 progression of most communicable diseases in the individual. As the spread and detection of
114 cases becomes a major challenge, emergency measures to be implemented remain
115 unavailable, including public health services, vaccination, communicable disease prevention
116 and control measures and surveillance, making epidemics more likely, more difficult to detect
117 and more difficult to control [35,36].

118

119 **Review methods**

120 For this review, we searched PubMed/Medline, Google Scholar and African Journals for
121 articles written in French and in English on bacterial resistance to antibiotics in DR Congo.
122 We used the search terms “bacterial resistance”, “antibiotic and resistance”, “antimicrobial
123 resistance”, “microbial resistance”, “susceptibility”, “resistance” combined with the name of
124 Democratic Republic of Congo. We screened the search results for relevant, methodologically
125 rigorous studies and conducted a forward search of the references of many of the relevant
126 results to identify additional studies. Articles were reviewed and publications using original
127 data on antibiotics resistance in humans and environment samples were included. The studies
128 site, study period, organism isolated, the resistance phenotype observed, the molecular
129 methodology used as well as the antimicrobial resistance genes found were appraised and
130 analysed. This review on antibacterial resistance in DRC focuses on available published
131 literature on the subject dating from 1990 to December 31st, 2019.

132

133 **Resistance pattern among Gram-negative and Gram-positive bacteria**

134 *Enterobacteriaceae:*

135 For *Enterobacteriaceae*, the emergence and spread of CTX-M type ESBLs are global, with
136 the highest prevalence observed in low-income countries, particularly in the community with
137 an estimated carrying prevalence of 70%, 35% and 15% respectively in Asia, the Eastern
138 Mediterranean Basin and Africa [24].

139 *Salmonella*

140 *Salmonella* spp. is the most studied bacterial genus in DRC as a result of the research
141 set up and is still ongoing since 2008 on bacteremia. Indeed, since the first publications on
142 bacteremia, the prevalence of resistance to ampicillin, chloramphenicol and cotrimoxazole are
143 particularly high (90 – 100%) [37,38]. The most frequently isolated species are *Salmonella*
144 *enteritidis*, *Salmonella typhimurium* and *Salmonella* Typhi. The level of resistance is as high
145 for *S. Typhi* as it is for non-Typhi *Salmonella* (NTS). Ampicillin, chloramphenicol and
146 cotrimoxazole are no longer susceptible in more than 70% of isolates [38,39,40]. For
147 Muyembe et al. in 2009, all isolates (11 isolates) of *S. Typhi* were resistant to ampicillin and
148 cotrimoxazole [41]. Finally, a decreased susceptibility to ciprofloxacin was also observed
149 between 59 to 65% [42,43,44]. Several resistance genes were detected in *Salmonella* spp.
150 strains isolated from DRC including, *bla*_{TEM-1b} and *bla*_{SHV-2a} genes [27,37,43]. Moreover, *S.*
151 *Typhi* harboring *bla*_{CTX-M} genes has been described in blood cultures in a bacteremic patient in
152 2018 [45]. Resistance to chloramphenicol, aminoglycosides, quinolones and sulfonamides is
153 correlated to the presence of *catA1*, *strA/B*, *sul1*, *dfrA1* genes and the *aac(6')-Iaa* gene
154 [37,40]. Some mutations on *gyrA* gene, as well as the presence of *qnrB1* and *aac(6')-Ib-cr*
155 genes were found in strains resistant to fluoroquinolones (Table 1 and Table 2). Puyvelde et

156 al., in 2019, analysed the entire genome of 81 strains of *S. typhimurium* by high-throughput
157 sequencing. They reported that 67% of the isolates (54/81) were ESBL-producers and 63%
158 were multidrug resistant (MDR), according to the definition used for *Salmonella* spp., i.e.
159 resistant to both ampicillin, chloramphenicol and cotrimoxazole. Several resistances genes
160 were found, including *catA*, *bla*_{TEM-1}, *bla*_{SHV-2A}, *dfrA*, *dfrA1*, *dfrA14*, *mphA* and a mutation in
161 the *gyrA* gene (S83Y) [46]. Bieke et al., in 2019, analysed 295 *S. Typhi*, 93 of which were
162 sequenced (WGS): 38.4% (114/295) were resistant to ampicillin, chloramphenicol and
163 cotrimoxazole; 24.5% (73/295) had decreased sensitivity to ciprofloxacin, mainly due to
164 mutations detected in the *gyrA* (S83E, S83Y, D87Y, D87G, A119E) and *gyrB* (E466D,
165 S464Y) genes [47].

166 *Escherichia coli*

167 *E. coli* is one of the most isolated microorganisms in bacteriology laboratories. A
168 single emerging clonal group of *E. coli*, designated sequence type 131 (ST131) by multilocus
169 sequence typing, has been identified as a factor in the AMR epidemic in *E. coli*, especially for
170 first-line agents such as fluoroquinolones and extended-spectrum cephalosporins. *E. coli*
171 contains a wide array of genetic diversity, most notably among genes that confer virulence
172 and resistance [48,49]. In DRC, five studies carried out in 2001, 2014 and 2015 showed that
173 the resistance rates of *E. coli* varied from 65 to 90% to penicillin [42,50,51], from 6 to 15% to
174 ceftriaxone and 15.4% to 31.5% to ciprofloxacin [52,53]. For studies in which resistance
175 genes were sought, the *bla*_{CTX-M-15} and *bla*_{SHV-18} genes were reported (Table 1) [53,54]. In
176 Bukavu, a recent study conducted in 2019 by Irengue et al. using whole genome sequencing of
177 21 *E. coli* strains showed that 33% of the strains (7 out of the 21 *E. coli*) belonged to ST131
178 and exhibited more virulence genes as compared to compared to the same clone in the NCBI
179 database. The majority of ESBL genes included *bla*_{CTX-M-15} and *bla*_{SHV-12} in all the isolates.

180 Several other AMR genes have been found including *bla*_{OXA-1}, *bla*_{TEM-1}, as well as genes
181 encoding resistance to aminoglycosides, quinolones, chloramphenicol, rifampicin,
182 tetracyclines and sulfonamides. As a matter of fact, *bla*_{CTX-M-15} gene is the most frequently
183 found ESBL gene among African hospital strains [55,56].

184 ***Klebsiella pneumoniae***

185 *K. pneumoniae* is a frequent cause of nosocomial infections and has also emerged as an
186 agent of severe community-acquired infections, including pyogenic liver abscess, pneumonia,
187 and meningitis. *K. pneumoniae* clinical isolates are evolving toward increasing levels of
188 antimicrobial drug resistance, placing this species among the infectious bacterial pathogens
189 that are most challenging to control [57]. In a study on urinary tract infection aetiologies in
190 Bukavu, Leonid et al. found that *K. pneumoniae* was the second most frequently identified
191 microorganism after *E. coli* [53]. Its resistance profile in studies published in the DRC in 2012
192 and 2015 showed a resistance rate of less than 35% for both amoxicillin/clavulanate acid
193 (14%-19%), ceftriaxone (14% -19%) and ciprofloxacin (12%-33%). One out of the 21 strains
194 of *K. pneumoniae* was phenotypically resistant to imipenem. No further studies were
195 performed to screen for the carbapenemase genes. Studies have shown that the use of
196 carbapenems promotes the emergence of carbapenemase-producing isolates. In Bukavu, the
197 use of these molecules is increasingly becoming part of the therapeutic arsenal of clinicians
198 [58]. The resistance genes described for *K. pneumoniae* in DRC are the *bla*_{CTX-M-15} and
199 *bla*_{SHV-18} genes, as previously reported for *E. coli* [52,54,59].

200 **Others Gram-negative bacteria (including non-fermenting rods)**

201 The available data do not allow the resistance profile of these other bacteria to be
202 established, given the small number of isolates tested (Table 2). Those microorganisms are
203 *Citrobacter freundii*, *Enterobacter* spp., and *Proteus* spp. *Enterobacter cloacae* is an

204 opportunistic pathogen that can cause several types of infections in the lower respiratory tract,
205 surgical sites, urinary tract and central nervous system. Moreover, this species is frequently
206 associated with nosocomial infections during outbreaks, emphasizing the need for rapid
207 detection and typing of such pathogens. *C. freundii* is considered a commensal of the
208 intestinal tract of humans and other animals. However, this species can also cause diarrhea
209 and other infections in humans [60,61]. De Boeck et al. in Kinshasa reported the presence of
210 *bla*_{CTX-M-15}, *bla*_{SHV-18} and *bla*_{SHV-2-like} genes in *C. freundii* and *E. cloacae* strains,
211 demonstrating that the two ESBL genes are widely disseminated in *Enterobacteriaceae*
212 [54,59]. In a recent study conducted by Leonid et al., out of the 78 analysed strains of *Vibrio*
213 *cholerae*, all were resistant to cotrimoxazole and nalidixic acid, 12% (9/78) had reduced
214 susceptibility to ciprofloxacin and 14% (11/78) were resistant to ampicillin. They were still
215 sensitive to chloramphenicol and tetracyclines. Many AMR genes were detected (Tab. 1) [62].
216 Finally, there are no data available on the occurrence and resistance profile of non-fermenting
217 Gram-negative bacilli in RDC.

218 **Resistance pattern among Gram-positive bacteria**

219 ***Staphylococcus aureus***

220 *S. aureus* is one of major human pathogens, associated with wide spectrum of
221 localized or systemic infections including wound infections, osteomyelitis, food poisoning,
222 endocarditis, as well as more serious illnesses, such as pneumonia and bacteremia [63,64]. In
223 RDC, the prevalence of bacterial infections caused by methicillin-resistant *S. aureus* (MRSA)
224 varied from 16 to 64% [28,44,65,66,67], which is similar to the prevalence reported in other
225 African countries [68]. The reported prevalences of antibiotics resistance are as follows: 33 to
226 72 % against to tetracyclines, 5 to 54 % against cotrimoxazole, 31 % against gentamicin, 26 to
227 69% against erythromycin and 20 to 59% against ciprofloxacin [28,44,66].

228 ***Streptococcus pneumoniae***

229 *S. pneumoniae* is the leading cause of pneumonia and bacterial meningitis. It is
230 commonly encountered in children and in immunocompromised and elderly populations and
231 it has considerable implications for healthcare systems worldwide [69]. To date, multidrug-
232 resistant *S. pneumoniae* (MDR-SP) have been isolated from both adults and children around
233 the world. These isolates are resistant to penicillin, clindamycin, cotrimoxazole and
234 erythromycin [70]. In DRC, a study performed on 23 *S. pneumoniae* isolates, showed that the
235 prevalence of penicillin resistance was 34%, 21% to cotrimoxazole and 13% to cefuroxime
236 (Table 2) [71]. Serotyping had not been completed, yet it would give us valuable information
237 on circulating strains depending on the vaccine used. A recent study of 163 nasal carriage
238 isolates of *S. pneumoniae* in children under 60 months of age reported 62% (n=101) of
239 resistance to penicillin G, 42% (n=68) to ampicillin, and 37% (n=61) to ceftriaxone. Almost
240 all strains were resistant to cotrimoxazole (94%) and 43% (n=70) were resistant to more than
241 three classes of antibiotics [72].

242 **Perspectives**

243 Surrounded by nine neighboring countries, the DRC faces many security and health
244 challenges, including population movement, high mortality rates and recurrent endemic
245 diseases, which make it impossible for the health system to make antibiotic resistance a
246 priority. With an annual budget of about US\$6 billion, 1.2% of which is allocated to the
247 health sector, for a population estimated at 85 million [73]. Despite the existence of 39
248 officially recognized medical schools, most of which are located in urban areas, the training
249 of clinical microbiologists remains a real problem because entirely self-financed, so that the
250 number of microbiologists is very low in relation to actual needs [29]. The DRC is almost last
251 with its human development index (168/169), public spending on health is among the lowest

252 with two dollars per capita. In this context of advanced poverty, investment in laboratory
253 materials and other diagnostic equipments for infectious diseases is therefore impossible. The
254 WHO recommends a minimum of \$35 per capita to safeguard a country's population [74]. Out
255 of the 424 hospitals in the country, very few have organized a microbiology service due to
256 lack of electricity, infrastructure and especially qualified personnel, as the only university in
257 the country that trains them markets 2 to 4 clinical microbiologists per year [75]. The serious
258 threat of antibiotic resistance in the DRC is the ineffectiveness of the antibacterial molecules
259 available on the market, which means that the use of old molecules which prove to be more
260 active with multidrug resistant isolates elsewhere should quickly orient the regulatory
261 authorities to change procurement policies.

262 In light of these challenges, there is an urgent need to create collaborative networks
263 with all microbiology laboratories across the country, which will then be linked to external
264 laboratories to effectively address the AMR problem.

265

266 **Conclusion**

267 This review summarizes the current state of our knowledge regarding antimicrobial
268 susceptibility of the common organisms causing serious community and hospital-acquired
269 infections in DRC. Many studies focused on *Salmonella* spp., *S. aureus* and *V. cholerae*.
270 Bacterial resistance to antibiotics concerns both Gram negative and Gram-positive bacteria.
271 Multidrug resistance prevalence is almost common in half of *S. pneumoniae* isolates. More
272 disturbing, we can note a worrying prevalence of MRSA with co-resistance to several other
273 antibiotics, and of ESBL-producers in *Enterobacteriaceae* with the diffusion of *bla*_{CTX-M-15} and
274 *bla*_{SHV-18} genes. Data on non-fermenting Gram negative bacilli, as well as carbapenem and
275 colistin resistance, are not available.

276 **Ethical issues**

277 There are no ethical concerns with this paper and ethical review board approval was
278 not required as no human subjects were involved.

279 **Financial support**

280 This work was supported by the French Government under the « Investissements
281 d’avenir » (Investments for the Future) program managed by the Agence Nationale de la
282 Recherche (ANR, fr: National Agency for Research), (reference: Méditerranée Infection 10-
283 IAHU-03). This work was supported by Région Provence-Alpes-Côte d’Azur and European
284 funding FEDER PRIM1.

285

286 **Transparency declaration:**

287 The authors declare no conflict of interest.

288

- 290 [1] Tadesse BT , Ashley EA, Ongarello S, Havumaki J, Wijegoonewardena M et al. Antimicrobial
 291 resistance in Africa: a systematic review. *BMC Infectious Diseases* (2017) 17:616 DOI
 292 10.1186/s12879-017-2713-1
- 293 [2] Van Duin D and Doi Y. The global epidemiology of carbapenemase-producing
 294 *Enterobacteriaceae*. *Virulence* 2017, VOL. 8, NO. 4, 460–469
- 295 [3] Xian-Zhi L, Plésiat P and Nikaido H. The Challenge of Efflux-Mediated Antibiotic Resistance
 296 in Gram-Negative Bacteria. *Clin Microbiolo Rev*. 2015 Apr; 28(2): 337–418
- 297 [4] Mshana ES, Matee M and Rweyemamu M. Antimicrobial resistance in human and animal
 298 pathogens in Zambia, Democratic Republic of Congo, Mozambique and Tanzania: an urgent
 299 need of a sustainable surveillance system. *Annals of Clinical Microbiology and Antimicrobials*
 300 2013, 12:28
- 301 [5] Pitout, J. D. D. (2018) Transmission Surveillance for Antimicrobial-Resistant Organisms in
 302 the Health System. *Microbiology Spectrum*, 6(5). doi:10.1128/microbiolspec.mtbp-0010-2016
- 303 [6] Mendelson M, Brink A, Gouws J, Mbelle N, Naidoo Vet al. (2018) The One Health
 304 stewardship of colistin as an antibiotic of last resort for human health in South Africa. *The*
 305 *Lancet Infectious Diseases*, 18(9), e288–e294
- 306 [7] Wong G, Brennan N, Mattick K, Pearson M, Briscoe S et al. Interventions to improve
 307 antimicrobial prescribing of doctors in training: the IMPACT (Improving Antimicrobial
 308 prescribing of doctors in Training) realist review. *BMJ Open*. 2015; 5(10): e009059.
- 309 [8] Guardabassi, L. (2017). Antimicrobial resistance: a global threat with remarkable geographical
 310 differences. *New Zealand Veterinary Journal*, 65(2), 57 -
 311 59. doi:10.1080/00480169.2017.1270645
- 312 [9] Le Doare K, Bielicki J, Heath P T, and Sharland, M. (2014) Systematic Review of Antibiotic
 313 Resistance Rates among Gram-Negative Bacteria in Children With Sepsis in Resource-Limited
 314 Countries. *Journal of the Pediatric Infectious Diseases Society*, 4(1), 11–20.
- 315 [10] Huttner A, Harbarth S, Carlet J, Cosgrove S, Goossens H et al. Antimicrobial resistance: a
 316 global view from the 2013 World Healthcare-Associated Infections Forum. *Antimicrob Resist*
 317 *Infect Control*.2013;2:31
- 318 [11] Baron, S., Diene, S., & Rolain, J.-M. (2018). Human microbiomes and antibiotic resistance.
 319 Human Microbiome Journal. doi:10.1016/j.humic.2018.08.005
- 320 [12] Peterson E, Kaur P. Antibiotic Resistance Mechanisms in Bacteria: Relationships
 321 Between Resistance Determinants of Antibiotic Producers, Environmental Bacteria, and
 322 Clinical Pathogens. *Front Microbiol*. 2018 Nov 30;9:2928. doi: 10.3389/fmicb.2018.02928.
 323 eCollection 2018. Review
- 324 [13] Gbaguidi-Haore H, Dumartin C, L’Heriteau F, Pefau, M, Hocquet D et al. (2012) Antibiotics
 325 involved in the occurrence of antibiotic-resistant bacteria: a nationwide multilevel study
 326 suggests differences within antibiotic classes. *Journal of Antimicrobial Chemotherapy*, 68(2),
 327 461–470.
- 328 [14] Drancourt M. (2016) Antiquité de la résistance aux antibiotiques. *Journal Des Anti-Infectieux*,
 329 18(2), 40–44.
- 330 [15] Pehrsson EC, Forsberg KJ, Gibson KM, Ahmadi S, Dantas G et al. Novel resistance functions
 331 uncovered using functional metagenomic investigations of resistance reservoirs. *Front*
 332 *Microbiol*.2013;4:145.

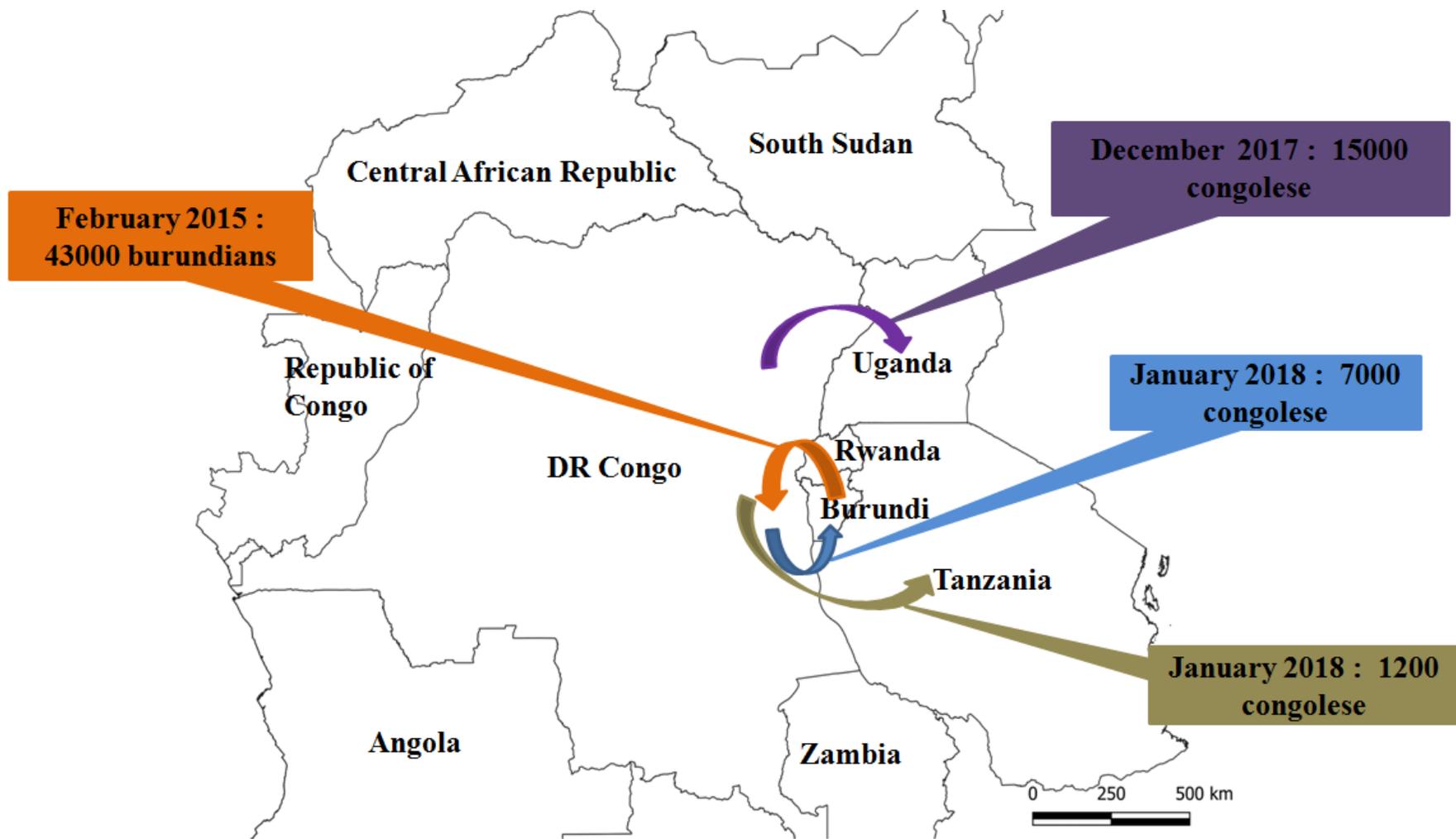
- 333 [16] Sommer M O, Church G M, and Dantas G. (2010) The human microbiome harbors a diverse
334 reservoir of antibiotic resistance genes. *Virulence*, 1(4), 299–303.
- 335 [17] Jarrell A S, Kruer R M, Berescu L D, Pronovost P J and Trivedi J B. (2018) Factors associated
336 with in-hospital mortality among critically ill surgical patients with multidrug-resistant
337 Gram-negative infections. *Journal of Critical Care*, 43, 321–326.
- 338 [18] Magiorakos AP, Srinivasan A, Carey R B, Carmeli Y, Falagas M E et al. (2012) Multidrug-
339 resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert
340 proposal for interim standard definitions for acquired resistance. *Clinical Microbiology and
341 Infection*, 18(3), 268–281.
- 342 [19] Corona F, Blanco P, Alcalde-Rico M, Hernando-Amado S, Lira F et al. (2016) The analysis of
343 the antibiotic resistome offers new opportunities for therapeutic intervention. *Future
344 Medicinal Chemistry*, 8(10), 1133–1151.
- 345 [20] Durão P, Balbontín R and Gordo I (2018) Evolutionary Mechanisms Shaping the Maintenance
346 of Antibiotic Resistance. *Trends in Microbiology*, 26(8), 677–691.
- 347 [21] Martinez J. L. (2014) General principles of antibiotic resistance in bacteria. *Drug Discovery
348 Today: Technologies*, 11, 33–39.
- 349 [22] Lee C-R, Cho I, Jeong B, and Lee S (2013) Strategies to Minimize Antibiotic Resistance.
350 *International Journal of Environmental Research and Public Health*, 10(9), 4274–4305.
- 351 [23] Armand-Lefèvre, L. (2017) La résistance en ville, mythe ou réalité ? La menace des
352 entérobactéries productrices de BLSE. *Journal Des Anti-Infectieux*, 19(1), 1–6.
- 353 [24] Mitgang A E , Hartley M D, Malchione MD, Koch M and Goodman J L , Review and Mapping
354 of Carbapenem-resistant *Enterobacteriaceae* in Africa: Using Diverse Data to Inform
355 Surveillance Gaps, *International Journal of Antimicrobial Agents* (2018) doi:
356 10.1016/j.ijantimicag.2018.05.019
- 357 [25] Baron S, Hadjadj L, Rolain J-M and Olaitan A O. (2016). Molecular mechanisms of polymyxin
358 resistance: knowns and unknowns. *International Journal of Antimicrobial Agents*, 48(6), 583–
359 591.
- 360 [26] Kariuki S and Dougan G (2014). Antibacterial resistance in sub-Saharan Africa: an
361 underestimated emergency. *Annals of the New York Academy of Sciences*, 1323(1), 43–55.
362 doi:10.1111/nyas.12380
- 363 [27] Kalonji LM, Post A, Phoba M-F, Falay D, Ngbonda D et al. (2015) Invasive *Salmonella*
364 Infections at Multiple Surveillance Sites in the Democratic Republic of the Congo, 2011–2014.
365 *Clinical Infectious Diseases*, 61(suppl 4), S346–S353.
- 366 [28] Phaku P, Lebughe M, Strauß L, Peters G, Herrmann M, Mumba et al. (2016) Unveiling the
367 molecular basis of antimicrobial resistance in *Staphylococcus aureus* from the Democratic
368 Republic of the Congo using whole genome sequencing. *Clinical Microbiology and Infection*,
369 22(7), 644.e1–644.e5.
- 370 [29] Stéphanie Stasse, Dany Vita, Jacques Kimfuta, Valéria Campos da Silveira, Paul Bossyns &
371 Bart Criel (2015) Improving financial access to health care in the Kisantu district in the
372 Democratic Republic of Congo: acting upon complexity, *Global Health Action*, 8:1, doi:
373 10.3402/gha.v8.25480
- 374 [30] Coghlan B, Brennan JR, Ngoy P, Dofara D Otto B, Clements M, Stewart T. Mortality in the
375 Democratic Republic of Congo ; a nationwide survey. *The Lancet*. volume 367, Issue 9504.
376 7-13 Janvier 2006, pages 44-51
- 377 [31] Gayer M, Legros D, Formenty P and Connolly MA. Conflict and Emerging Infectious
378 Diseases. *Emerging Infectious Diseases* · www.cdc.gov/eid · Vol. 13, No. 11, November 2007

- 379 [32] Casey SE, Gallagher MC, Rukengeza BM, Meyers JL, Vinas CM and Austin J. Care-Seeking
380 Behavior by Survivors of Sexual Assault in the Democratic Republic of the Congo. *Am J*
381 *Public Health*. 2011 June; 101(6): 1054–1055.
- 382 [33] Kohli A, Makambo MT, Ramazani P, Zahiga I, Safari O, Bachunguye R et al. A Congolese
383 community-based health program for survivors of sexual violence. *Confl Health*. 2012;6:6
- 384 [34] [http://www.unhcr.org/fr/news/briefing/2018/1/5a70632aa/violences-rdc-generent-hausse-](http://www.unhcr.org/fr/news/briefing/2018/1/5a70632aa/violences-rdc-generent-hausse-afflux-refugies-vers-lest.html)
385 [afflux-refugies-vers-lest.html](http://www.unhcr.org/fr/news/briefing/2018/1/5a70632aa/violences-rdc-generent-hausse-afflux-refugies-vers-lest.html)
- 386 [35] Hammer CC, Brainard J and Hunter. Risk factors and risk factor cascades for communicable
387 disease outbreaks in complex humanitarian emergencies: a qualitative systematic review. *BMJ*
388 *Glob Health*. 2018; 3(4) : e000647
- 389 [36] Connolly MA, Gayer M, Ryan MJ, Salama P, Spiegel P and Heymann DL. Communicable
390 diseases in complex emergencies: impact and challenges. *The Lancet*. 2004 Nov 27-Dec 3;
391 364(9449):1974-83.
- 392 [37] Leekitcharoenphon P, Friis C, Zankari E, Svendsen C A, Price L B, et al. (2013) Genomics of
393 an emerging clone of *Salmonella* serovar Typhimurium ST313 from Nigeria and the
394 Democratic Republic of Congo. *The Journal of Infection in Developing Countries*, 7(10).
- 395 [38] Ley B, Le Hello S, Lunguya O, Lejon V, Muyembe J-J et al. (2014) Invasive *Salmonella*
396 *enterica* Serotype Typhimurium Infections, Democratic Republic of the Congo, 2007–2011.
397 *Emerging Infectious Diseases*, 20(4), 701–704. doi:10.3201/eid2004.131488
- 398 [39] Vandenberg O, Nyarukweba D Z, Ndeba P M, Hendriksen R S, Barzilay E J, et al. (2010)
399 Microbiologic and Clinical Features of *Salmonella* Species Isolated From Bacteremic Children
400 in Eastern Democratic Republic of Congo. *Pediatr Infect Dis J* 2010; 29: 504 –510
- 401 [40] Phoba M-F, Boeck H, Ifeka B B, Dawili J, Lunguya O et al. (2013) Epidemic increase in
402 *Salmonella* bloodstream infection in children, Bwamanda, the Democratic Republic of Congo.
403 *European Journal of Clinical Microbiology & Infectious Diseases*, 33(1), 79–87.
- 404 [41] Muyembe-Tamfum J J, Veyi J, Kaswa M, Lunguya O, Verhaegen J et al. (2009) An outbreak of
405 peritonitis caused by multidrug-resistant *Salmonella* Typhi in Kinshasa, Democratic Republic
406 of Congo. *Travel Medicine and Infectious Disease*, 7(1), 40–43
- 407 [42] Bahwere P, Levy J, Hennart P, Donnen P, Lomoyo W et al. Community-Acquired Bacteremia
408 among Hospitalized Children in Rural Central Africa. *Int J Infect Dis* 2001; 5:180-188.
- 409 [43] Phoba M-F, Barbé B, Lunguya O, Masendu L, Lulengwa D et al. (2017) *Salmonella enterica*
410 serovar Typhi Producing CTX-M-15 Extended Spectrum β -Lactamase in the Democratic
411 Republic of the Congo. *Clinical Infectious Diseases*, 65(7), 1229–1231.
- 412 [44] Vandendriessche S, De Boeck H, Deplano A, Phoba M-F, Lunguya O et al. (2017)
413 Characterisation of *Staphylococcus aureus* isolates from bloodstream infections, Democratic
414 Republic of the Congo. *European Journal of Clinical Microbiology & Infectious Diseases*,
415 36(7), 1163–1171.
- 416 [45] Kakabadze E, Makalatia K, Grzelishvili N, Bakuradze N, Goderdzishvili M et al. (2018)
417 Selection of Potential Therapeutic Bacteriophages that Lyse a CTX-M-15 Extended Spectrum
418 β -Lactamase Producing *Salmonella enterica* Serovar Typhi Strain from the Democratic
419 Republic of the Congo. *Viruses*, 10(4), 172.
- 420 [46] Van Puyvelde, S., Pickard, D., Vandelannoote, K., Heinz, E., Barbé, B., de Block, T., ...
421 Deborggraeve, S. (2019). *An African Salmonella Typhimurium ST313 sublineage with*
422 *extensive drug-resistance and signatures of host adaptation*. *Nature Communications*,
423 10(1). doi:10.1038/s41467-019-11844-z

- 424 [47] Bieke Tack, Marie-France Phoba, Sandra Van Puyvelde, Lisette M. Kalonji, Liselotte Hardy,
425 Barbara Barbé et al. *Salmonella* Typhi From Blood Cultures in the Democratic Republic of the
426 Congo: A 10-Year Surveillance. *Clinical Infectious Diseases*® 2019;68(S2):S130–7
- 427 [48] Hutton T A, Innes G K, Harel J, Garneau P, Cucchiara A et al.(2017) Phylogroup and
428 virulence gene association with clinical characteristics of *Escherichia coli* urinary tract
429 infections from dogs and cats. *Journal of Veterinary Diagnostic Investigation*, 30(1), 64–70
- 430 [49] Johnson J R, Porter S, Thuras P and Castanheira M (2017). The Pandemic H30 Subclone of
431 Sequence Type 131 (ST131) as the Leading Cause of Multidrug-Resistant *Escherichia coli*
432 Infections in the United States (2011–2012). *Open Forum Infectious Diseases*, 4(2).
- 433 [50] Kadima MC, Mumba MA, Biayi MJ, Ntambwe KG, Mulowayi KF. Profil bactériologique de
434 l'infection urinaire gravidique (Cas de l'hôpital Bonzola à Mbuji-Mayi en RD Congo). *Rev.*
435 *méd. Madag.* 2015 ; 5(3): 626-633
- 436 [51] Liesse IJM, José Mulwahali WJ, Takaisi-Kikuni NB. Antimicrobial susceptibility patterns of
437 *enterobacteriaceae* isolated from HIV-infected patients in Kinshasa. *Pan African Medical*
438 *Journal.* 2014; 17:179
- 439 [52] Irengé L M, Kabego L, Kinunu FB, Itongwa M, Mitangala PN et al (2015) Antimicrobial
440 resistance of bacteria isolated from patients with bloodstream infections at a tertiary care
441 hospital in the Democratic Republic of the Congo. *South African Medical Journal*, 105(9), 752
- 442 [53] Irengé LM, Kabego L, Vandenberg O, Chirimwami BR and Gala JL(2014) Antimicrobial
443 resistance in urinary isolates from inpatients and outpatients at a tertiary care hospital in
444 South-Kivu Province (Democratic Republic of Congo) *BMC Research Notes* 2014, 7:374
- 445 [54] De Boeck H, Miwanda B, Lunguya-Metila O, Muyembe-Tamfum J-J, Stobberingh E et al.
446 (2012) ESBL-Positive Enterobacteria Isolates in Drinking Water. *Emerging Infectious*
447 *Diseases*, 18(6)
- 448 [55] Alonso C A, Zarazaga M, Ben Sallem R, Jouini A, Ben Slama K et al. (2017) Antibiotic
449 resistance in *Escherichia coli* in husbandry animals: the African perspective. *Letters in*
450 *Applied Microbiology*, 64(5), 318–334
- 451 [56] Irengé LM, Ambroise J, Bearzatto B, Durant J-F, Chirimwami RB & Gala J-L (2019). Whole-
452 genome sequences of multidrug-resistant *Escherichia coli* in South-Kivu Province,
453 Democratic Republic of Congo: characterization of phylogenomic changes, virulence and
454 resistance genes. *BMC Infectious Diseases*, 19(1). doi:10.1186/s12879-019-3763-3
- 455 [57] Bialek-Davenet S, Criscuolo A, Ailloud F, Passet V, Jones L et al. Genomic definition of
456 hypervirulent and multidrug-resistant *Klebsiella pneumoniae* clonal groups. *Emerg Infect Dis.*
457 2014 Nov
- 458 [58] Harris P N A, Tambyah P A, Lye D C, Mo Y, Lee T H et al. (2018) Effect of Piperacillin-
459 Tazobactam vs Meropenem on 30-Day Mortality for Patients With *E coli* or *Klebsiella*
460 *pneumoniae* Bloodstream Infection and Ceftriaxone Resistance. *JAMA*, 320(10), 984.
- 461 [59] De Boeck H, Lunguya O, Muyembe J-J, Glupczynski Y and Jacobs J. (2012) Presence of
462 extended-spectrum beta-lactamase-producing *Enterobacteriaceae* in waste waters, Kinshasa,
463 the Democratic Republic of the Congo. *European Journal of Clinical Microbiology &*
464 *Infectious Diseases*, 31(11), 3085–3088.
- 465 [60] Yang L, Li P, Liang B, Hu X, Li J et al. (2018) Multidrug-resistant *Citrobacter freundii* ST139
466 co-producing NDM-1 and CMY-152 from China. *Scientific Reports*, 8(1).
- 467 [61] Liu L, Hao S, Lan R, Wang G, Xiao D et al. (2015) The Type VI Secretion System Modulates
468 Flagellar Gene Expression and Secretion in *Citrobacter freundii* and Contributes to Adhesion
469 and Cytotoxicity to Host Cells. *Infection and Immunity*, 83(7), 2596–2604

- 470 [62] Leonid M. Irengé, Jérôme Ambroise, Prudence N. Mitangala, Bertrand Bearzatto, Raphaël
471 K.S. Kabangwa, Jean-François Durant et al. Genomic analysis of pathogenic isolates of *Vibrio*
472 *cholerae* from eastern Democratic Republic of the Congo (2014-2017)
473 bioRxiv 708735; doi: <https://doi.org/10.1101/708735>
- 474 [63] Ilcyszyn WM, Sabat A J, Akkerboom V, Szkarlat A, Klepacka J et al. (2016) Clonal Structure
475 and Characterization of *Staphylococcus aureus* Strains from Invasive Infections in Paediatric
476 Patients from South Poland: Association between Age, spa Types, Clonal Complexes, and
477 Genetic Markers. *PLOS ONE*, 11(3), e0151937.
- 478 [64] Asadollahi P, Farahani N N, Mirzaii M, Khoramrooz S S, van Belkum A et al. (2018)
479 Distribution of the Most Prevalent Spa Types among Clinical Isolates of Methicillin-Resistant
480 and -Susceptible *Staphylococcus aureus* around the World: A Review. *Frontiers in*
481 *Microbiology*, 9.
- 482 [65] De Boeck H, Vandendriessche S, Hallin M, Batoko B, Alworonga J-P et al.(2015)
483 *Staphylococcus aureus* nasal carriage among healthcare workers in Kisangani, the Democratic
484 Republic of the Congo. *European Journal of Clinical Microbiology & Infectious Diseases*,
485 34(8), 1567–1572.
- 486 [66] Liesse IJM, José Mulwahali WJ, Mundu LC, Takaisi-Kikuni NB. High prevalence of
487 methicillin resistant *staphylococci* strains isolated from surgical site infections in Kinshasa.
488 *Pan African Medical Journal*. 2014; 18:322
- 489 [67] Lupande DM, Cirezi B, Ngoma PK, Itongwa M, Kashosi TM et al. Determinants of nasal
490 carriage of MRSA in Bukavu city. *International Journal of Bacteriology, Virology and*
491 *Immunology*. Vol. 3(3): pp 043-052, October, 2017
- 492 [68] Schaumburg F, Alabi A S, Peters G and Becker K (2014). New epidemiology of
493 *Staphylococcus aureus* infection in Africa. *Clinical Microbiology and Infection*, 20(7), 589–
494 596.
- 495 [69] Hirvonen J J, Seiskari T, Harju I, Rantakokko-Jalava K, Vuento R et al. (2015) Use of an
496 automated PCR assay, the GenomEra *S. pneumoniae*, for rapid detection of *Streptococcus*
497 *pneumoniae* in blood cultures. *Infectious Diseases*, 47(11), 796–800.
- 498 [70] Thummeepak R, Leerach N, Kunthalert D, Tangchaisuriya U, Thanwisai A et al. (2015) High
499 prevalence of multi-drug resistant *Streptococcus pneumoniae* among healthy children in
500 Thailand. *Journal of Infection and Public Health*, 8(3), 274–281.
- 501 [71] Kacou-Ndouba A, Revathi G, Mwathi P, Seck, A., Diop A et al. (2016) Results from the Survey
502 of Antibiotic Resistance (SOAR) 2011–14 in the Democratic Republic of Congo, Ivory Coast,
503 Republic of Senegal and Kenya. *Journal of Antimicrobial Chemotherapy*, 71(suppl 1), i21–
504 i31.
- 505 [72] Birindwa AM, Emgård M, Nordén R, Samuelsson E, Geravandi S, Gonzales-Siles L. et al.
506 (2018). High rate of antibiotic resistance among *pneumococci* carried by healthy children in
507 the eastern part of the Democratic Republic of the Congo. *BMC Pediatrics*,
508 18(1). doi:10.1186/s12887-018-1332-3
- 509 [73] Kongo Innocent Emmanuel. The Access to health care in the Democratic Republic of Congo:
510 Major challenge for the poor. *J Nursing Palliat serv*, 2016 Volume 1(1): 6-8
- 511 [74] Rajan D, Kalambay H, Mossoko M, Kwete D, Bulakali J, Lokonga, J.-P et al. (2014). Health
512 service planning contributes to policy dialogue around strengthening district health systems:
513 an example from DR Congo 2008-2013. *BMC Health Services Research*, 14(1).
514 doi:10.1186/s12913-014-0522-4

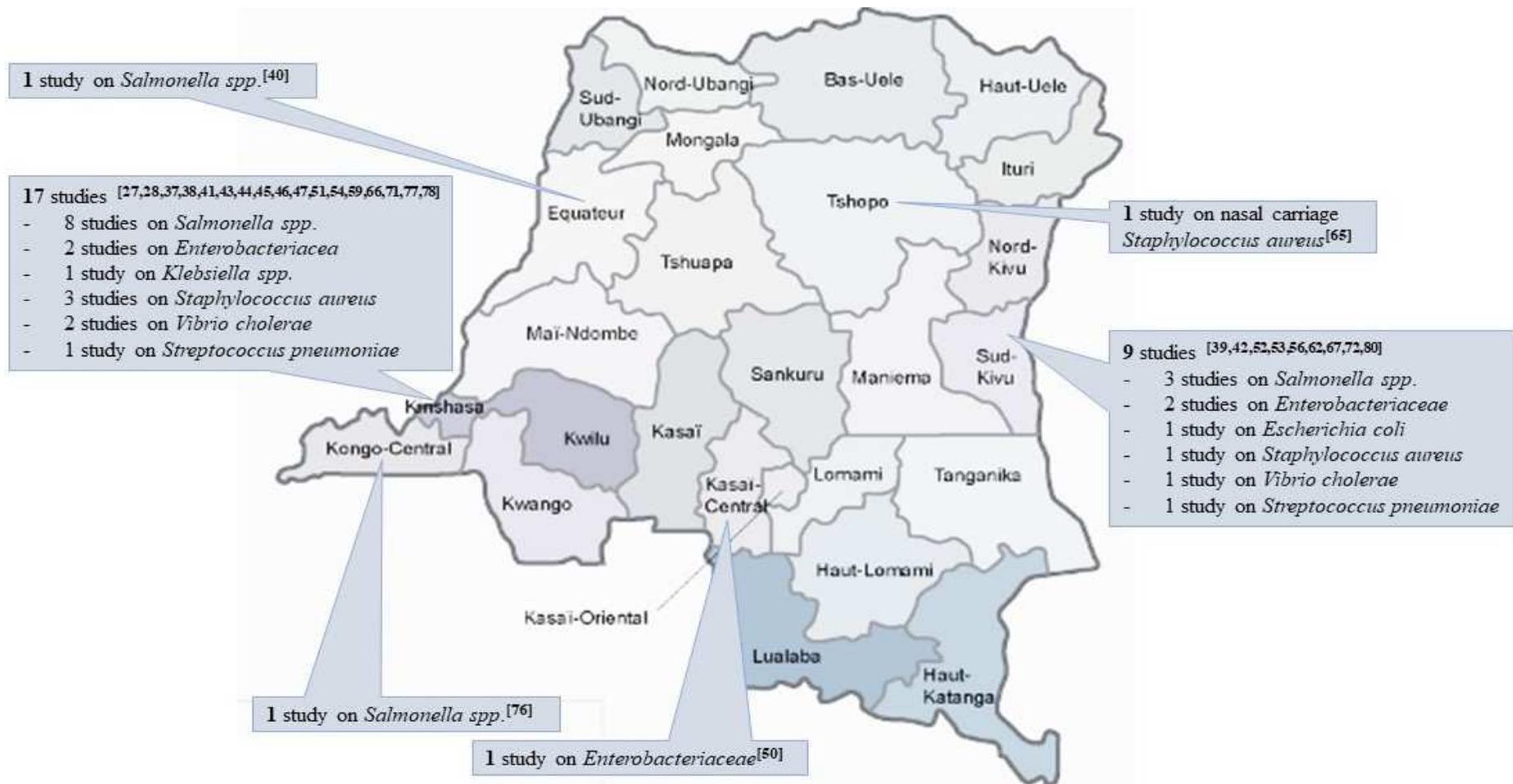
- 515 [75] Kalambay Ntembwa Hyppolite and Lerberghe Van Wim. The. Improving health systems
516 efficiency: Democratic republic of Congo; Improving aid coordination in the health sector
517 (world health report). World Health Organization; 2015. WHO/HIS/HGF/CaseStudy/15.4
- 518 [76] Green SDR and Cheesbrough JS (1993) *Salmonella* bacteraemia among young children at a
519 rural hospital in western Zaire, *Annals of Tropical Paediatrics*, 13:1, 45-53,
- 520 [77] Smith AM, Njanpop-Lafourcade B-M, Mengel MA, Gessner BD, Sauvageot D al. (2015)
521 Comparative Characterization of *Vibrio cholerae* O1 from Five Sub-Saharan African
522 Countries Using Various Phenotypic and Genotypic Techniques. *PLoS ONE* 10(11): e0142989.
- 523 [78] Miwanda B, Moore S, Muyembe J-J, Nguefack-Tsague G, Kabangwa I K et al. (2015)
524 Antimicrobial Drug Resistance of *Vibrio cholerae*, Democratic Republic of the Congo.
525 *Emerging Infectious Diseases*, 21(5), 847-851.
- 526 [79] Mapatano Mala Ali, Piripiri Lina, « Quelques erreurs courantes d'analyse d'un système
527 d'information sanitaire (RD Congo) », *Santé Publique*, 2005/4 (Vol. 17), p. 551-558. DOI :
528 10.3917/spub.054.0551. URL : [https://www.cairn.info/revue-sante-publique-2005-4-page-](https://www.cairn.info/revue-sante-publique-2005-4-page-551.htm)
529 [551.htm](https://www.cairn.info/revue-sante-publique-2005-4-page-551.htm)
- 530 [80] Mitima TK, Birindwa AM, Lupande DM, Mihuhi N, Kivukuto JM et al. (2018) Antibio-
531 résistance des souches de *Salmonella spp* isolées d'hémocultures à Bukavu en RD Congo. *Pan*
532 *African Medical Journal*. 2018;29:42.



533

534 **Figure 1:** Movement of population in the context of armed conflict in Eastern part of Democratic Republic of Congo.

535



536

537 **Figure 2:** Localization of published data on antimicrobial resistance in Democratic Republic of the Congo.

538

539 **Table 1:** Main antimicrobial resistance genes found in Democratic Republic of Congo

540

Species	Methods	N° of strains	Antibiotic resistance genes	References
<i>Salmonella</i> spp.	PCR, gene sequencing, whole genome sequencing	453	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{SHV-2a} , <i>mph(A)</i> , <i>gyrA</i> mutation, <i>qnrB1</i> , <i>aac(6')-Ib-cr</i> , <i>bla</i> _{TEM-1} , <i>bla</i> _{TEM-1b} , <i>catA1</i> , <i>strA/B</i> , <i>sull</i> , <i>dfrA1</i> , <i>aac(6')-Iaa</i>	[27,37, 38, 40, 43,45,47,77]
<i>E. coli</i>	PCR, Whole genome sequencing	21	<i>bla</i> _{CTX-M-1} , <i>bla</i> _{TEM} , <i>bla</i> _{CMY} , <i>bla</i> _{OXA} , <i>aac3</i> , <i>ant2''</i> , <i>ant3''</i> , <i>aph3''</i> , <i>aph6</i> , <i>pbp2</i> , <i>aac6'</i> , <i>qnrB</i> , <i>mphA</i> , <i>cat</i> , <i>catA</i> , <i>catB</i> , <i>arr</i> , <i>folp</i> , <i>sull</i> , <i>sullI</i> , <i>tetA</i> , <i>tetB</i> , <i>tetD</i> , <i>dhfr</i>	[53,56]
<i>Klebsiella</i> spp.	PCR	3	<i>bla</i> _{CTX-M-15} , <i>bla</i> _{SHV} variants	[59]
<i>S. aureus</i>	PCR, Whole genome sequencing	148	<i>aac(6')-aph(2'')</i> , <i>tetK</i> , <i>emrC</i> , <i>mecA</i> gene found, mutation in <i>femA</i> gene found, <i>dfrG</i> , <i>rpoB</i> , <i>emrC</i>	[28,44]
<i>Vibrio cholerae</i>	Whole genome sequencing	78	<i>cardB</i> , <i>intSXT</i> , <i>sxt/R391</i> , <i>sullI</i> , <i>sull</i> , <i>qnrVC</i> , <i>aph3-dprime</i> , <i>aph6</i> , <i>drfA</i> , <i>dhfr</i> , <i>flor</i> , <i>gyrA</i> (S83I), <i>parC</i> (S85L)	[46]

Table 2. Prevalence of resistance among bacteria isolated in Democratic Republic of Congo

Study period	Microorganism isolated (year of isolation)	Prevalence of resistance % (N)	Gene identified	References
1993	<i>Salmonella</i> spp.(1986)	90% (n=90) of resistance to ampicillin, chloramphenicol, streptomycin and tetracycline	ND ^a	[76]
2001	<i>Salmonella</i> spp. and <i>E. coli</i> (1990)	100% of resistance to ampicillin and chloramphenicol for <i>S. enteritidis</i> , 65% (n=46) of resistance to ampicillin and chloramphenicol for <i>E. coli</i> (n=19)	ND	[42]
2009	<i>Salmonella</i> Typhi (2005)	All the strains (n=11) exhibited resistance to ampicillin (>256 mg/L) and cotrimoxazole (>32 mg/L)	ND	[41]
2010	<i>Salmonella</i> spp.(2006)	For <i>S. typhimurium</i> , high proportion of isolates were resistant to ampicillin (85.7%), chloramphenicol (92.5%), and cotrimoxazole (94.7%), 6.1% of <i>S. enteritidis</i> tested were resistant to nalidixic acid and ciprofloxacin, 10.2% of <i>S. enteritidis</i> isolates were resistant to gentamicin. 89.7% of <i>S. Typhi</i> isolates presented a similar antimicrobial resistant profile as the one observed among NTS ^b	Two isolates displayed resistance to cefoxitin (32mg/L); the presence of the genes <i>bla</i> _{CMY-1} , <i>bla</i> _{CMY-2} , <i>bla</i> _{ACC} , <i>bla</i> _{CTX-M} , and <i>bla</i> _{TEM} was negative	[39]
2013	<i>Salmonella typhimurium</i> (2006)	100% (n=11) of resistance to ampicillin, cotrimoxazole, and chloramphenicol	<i>bla</i> _{TEM-1b} , <i>catA1</i> , <i>strA/B</i> , <i>sul1</i> , <i>dfrA1</i> , <i>aac(6')-Iaa</i>	[37]
2014	<i>Salmonella</i> spp. (2011)	96% (n=180) of resistance to ampicillin; chloramphenicol and cotrimoxazole,	<i>bla</i> _{SHV-2a} , <i>mph(A)</i>	[38]
2014	<i>Salmonella</i> spp. (2012)	72.2% (n=18) of <i>S. Typhi</i> isolates showed co-resistance to ampicillin and cotrimoxazole, 33.3% showed additional resistance to chloramphenicol and hence were MDR ^c . 97.6% (n=85) of NTS isolates were MDR; 1.0 % <i>S. typhimurium</i> isolate had additional DCS ^d	<i>gyrA</i> gene mutation found	[40]
2015	<i>Salmonella</i> spp. (2014)	<i>S. Typhi</i> isolates (n=164), MDR and DCS rates were 37.8%	<i>gyrA</i> mutation found, <i>qnrB1</i> , <i>aac(6')</i> -	[27]

		and 37.2%, respectively. MDR were 90.2% and 79.7%, respectively for <i>S. typhimurium</i> (386) and <i>S. enteritidis</i> (390). ESBL production was observed in 12.7% of <i>S. typhimurium</i> isolates	<i>Ib-cr</i> , <i>bla</i> _{TEM-1}	
2017	<i>Salmonella</i> Typhi (2015)	Production of ESBL ^e was confirmed by PCR, the first time in DR Congo on <i>S. Typhi</i> . The isolate further showed decreased ciprofloxacin to pefloxacin and nalidixic acid with resistance	<i>bla</i> _{CTX-M-15}	[43]
2018	<i>Salmonella</i> Typhi (2017)	ESBL-producing <i>S. Typhi</i> isolate with a decreased ciprofloxacin susceptibility	<i>bla</i> _{CTX-M-15}	[45]
2018	<i>Salmonella</i> spp. (2014)	27% (n=60) of resistance to cefuroxime, 20% to ceftriaxone and norfloxacin	ND	[80]
2019	<i>Salmonella typhimurium</i> (2016)	67% (54/81) were ESBL producers and 63% were MDR (resistance both to ampicillin, chloramphenicol and cotrimoxazole).	<i>catA</i> , <i>bla</i> _{TEM-1} , <i>dfrA</i> , <i>dfrA1</i> , <i>dfrA14</i> , <i>bla</i> _{SHV-2A} , <i>mphA</i> , <i>gyrA</i> mutation (S83Y)	[46]
2019	<i>Salmonella</i> Typhi (2017)	38.4% (114/295) were resistant to ampicillin, chloramphenicol and cotrimoxazole; 24.5% (73/295) had decreased sensitivity to ciprofloxacin	<i>gyrA</i> (S83E, S83Y, D87Y, D87G, A119E), <i>gyrB</i> (E466D, S464Y)	[47]
2012	<i>Enterobacteriaceae</i> (2011)	7.4% (n=190) ESBL-producing <i>Enterobacteriaceae</i>	<i>bla</i> _{CTX-M-1} group	[59]
2014	<i>Enterobacteriaceae</i> and Non fermenting Gram-negative rods (2013)	16.3% (n=643) of isolates displayed a MDR phenotype; 80% (n=25) of isolates were ESBL-producers	<i>bla</i> _{CTX-M-1} group	[53]
2014	<i>Enterobacteriaceae</i> (2013)	100% (n=79) of resistance to tetracycline, over 90% of resistance to ampicillin, cotrimoxazole and chloramphenicol and over 65% of resistance to norfloxacin	ND	[51]

2015	<i>Enterobacteriaceae</i> (2014)	100% (n=112) of resistance to cotrimoxazole, 67-100% of resistance to ampicillin and > 50% of them were ESBL producers	ND	[52]
2015	<i>Enterobacteriaceae</i> and Gram-positive cocci (2015)	98% (n=38) of <i>E. coli</i> and 65% (n=22) of <i>S. aureus</i> resisted to penicillin, and 92% of <i>E. coli</i> and 73% of <i>S. aureus</i> resisted to cefotaxime	ND	[50]
2012	<i>Klebsiella</i> spp. and <i>E. aerogenes</i> (2010)	5.3% (150) of ESBL producers (8 isolates).	5 <i>bla</i> _{CTX-M} genes and 3 <i>bla</i> _{SHV} variants	[54]
2019	<i>Escherichia coli</i> (2014)	All isolates were MDR corresponding to ESBL producers (n=21). Twenty-one (21/21) and 19/21 strains were susceptible to imipenem and amikacin, respectively	<i>bla</i> _{CTX-M-1} , <i>bla</i> _{TEM} , <i>bla</i> _{CMY} , <i>bla</i> _{OXA} , <i>aac3</i> , <i>ant2''</i> , <i>ant3''</i> , <i>aph3''</i> , <i>aph6</i> , <i>pbp2</i> , <i>aac6'</i> , <i>qnrB</i> , <i>mphA</i> , <i>cat</i> , <i>catA</i> , <i>catB</i> , <i>arr</i> , <i>folP</i> , <i>sulI</i> , <i>sulIII</i> , <i>tetA</i> , <i>tetB</i> , <i>tetD</i> , <i>dhfr</i>	[56]
2014	<i>Staphylococcus</i> spp.(2013)	63.5% (n=74) of <i>S. aureus</i> and 90% (n=15) of CNS ^f were MRSA ^g and MR-CNS, respectively	ND	[66]
2015	<i>Staphylococcus aureus</i> (2011)	16% (n=63) of MRSA	ND	[65]
2016	<i>Staphylococcus aureus</i> (2014)	33% (n=100) were MRSA, 72% of resistance to cyclins and 54% of resistance to cotrimoxazole	<i>mecA</i> , mutation in <i>femA</i> gene found, <i>dfrG</i> , <i>rpoB</i> , <i>emrC</i>	[28]
2017	<i>Staphylococcus aureus</i> (2016)	36% (n=45) of isolates were MRSA	ND	[67]
2017	<i>Staphylococcus aureus</i> (2013)	25% (n=108) were MRSA, 31% were resistant to aminoglycosides, 26 % to macrolides and 20 % to ciprofloxacin	<i>aac(6')-aph(2'')</i> , <i>tetK</i> , <i>emrC</i>	[44]
2015	<i>Vibrio cholerae</i> (2013)	98% (n=36) of resistance to cotrimoxazole, 71% to nitrofurantoin and 18% to nalidixic acid.	ND	[77]
2015	<i>Vibrio cholerae</i> (2012)	Although sensitivity to fluoroquinolones seemed to be preserved, strain resistance patterns continued to evolve with	MLVA genotyping, no resistance genes searched	[78]

		the circulation of isolates resistant to tetracyclines and ampicillin from 2007 to 2010, and displayed a single antimicrobial drug susceptibility profile: resistance to most antimicrobial drugs (chloramphenicol, erythromycin, cotrimoxazole) except cyclines and fluoroquinolones.		
2019	<i>Vibrio cholerae</i> (2017)	100% (n=78) of resistance and nalidixic acid, 12% and 14% of resistance to ciprofloxacin and ampicillin, respectively	<i>cardB</i> , <i>IntSXT</i> , <i>sxt/R391</i> , <i>sullI</i> , <i>sullI</i> , <i>qnrVC</i> , <i>aph3-dprime</i> , <i>aph6</i> , <i>drfA</i> , <i>dhfr</i> , <i>flor</i> , <i>gyrA</i> (S83I), <i>parC</i> (S85L),	[62]
2016	<i>Streptococcus pneumoniae</i> and <i>Haemophilus influenzae</i> (2014)	83% (n=23) of <i>S. pneumoniae</i> isolates were resistant to penicillin, 28% (n=23) of <i>H. influenzae</i> were resistant to amoxicillin/clavulanate acid	ND	[71]
2018	<i>Streptococcus pneumoniae</i> (2015)	70 out of the 163 isolates (43%) of the pneumococci were MDR (non-susceptible to ≥ 3 classes of antimicrobial agents, including the β -lactams).	ND (PCR done for serotyping only)	[72]

^a ND, not determined; ^b NTS: Non Typhi *Salmonella*; ^c MDR: multidrug resistant; ^d DCS: Decreased Ciprofloxacin Susceptibility; ^e ESBL: extended spectrum β -lactamase; ^f CNS: coagulase negative *Staphylococcus*; ^g MRSA: methicillin resistant *S. aureus*.