

Supplementary materials 2 – Study characteristics

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Table S1: Data availability for specific pathogen-bloodstream infection combinations based on comparator group

Table S1 - Number of comparisons of excess health risk associated with drug-resistance for bloodstream infections caused by six key pathogens, including comparator group, for any health outcome

Key resistant pathogen	Comparator group		Total
	Susceptible infection	Uninfected	
Carbapenem resistant <i>A. baumannii</i>	7	0	7
3rd gen. cephalosporin resistant Enterobacterales	2	1	3
Vancomycin resistant <i>E. faecium</i>	13	5	18
3rd gen. cephalosporin resistant <i>E. coli</i>	12	1	13
Carbapenem resistant <i>E. coli</i>	0	0	0
3rd gen. cephalosporin resistant <i>K. pneumoniae</i>	3	0	3
Carbapenem resistant <i>K. pneumoniae</i>	5	0	5
Carbapenem resistant <i>P. aeruginosa</i>	7	1	8
Methicillin resistant <i>S. aureus</i>	15	3	18
Total	64	11	75

Table S2: Non mortality outcomes data availability

Table S 2- Heatmap of the number of outcome records with excess health risk (other than mortality) associated with drug-resistance for bloodstream infections (BSIs) caused by six key pathogens, including any comparator group

	Pathogen /outcome	Clinical failure ¹	Organ failure	Acute respiratory distress syndrome	C. difficile infection ²	ICU admission	Need for hospitalization	Recurrence /relapse ¹	Physical disability
BSI	<i>A. baumannii</i>	0	0	0	0	0	0	1	0
	3GCR- <i>E. coli</i>	0	0	0	0	1	0	0	0
	CR- <i>E. coli</i>	0	0	0	0	0	0	0	0
	3GCR- <i>K. pneumoniae</i>	0	0	0	0	0	0	0	0
	CR- <i>K. pneumoniae</i>	0	0	0	0	0	0	0	0
	3GCR-Enterobacterales	0	0	0	0	0	0	1	0
	CR-Enterobacterales	0	0	0	0	0	0	0	0
	CR- <i>P. aeruginosa</i>	1	1	0	1	0	0	1	1 ²
	MRSA	0	1	0	0	1	0	2	0
	VRE	1	0	0	0	1	0	2	0
Total	Number of studies	2	2	0	1	3	0	7	1

¹Clinical failure and/or recurrence outcome data were pooled as a composite outcome for VRE BSI.

²Compared to uninfected patients, all the other studies compare to patients with susceptible infection.

3GCR - 3rd generation cephalosporin resistant, CR- carbapenem resistant, VRE Vancomycin resistant *E. faecium*, MRSA - Methicillin resistant *S. aureus*.

Table S3: Descriptive statistics of the studies included in the systematic review comparing drug-resistant to drug-susceptible bloodstream infections (BSIs)

Table S3 Descriptive statistics of patients included in the primary studies (N=56) assessing the excess health risk of drug-resistant bloodstream infections for six key pathogens, as identified through a systematic literature review (1990-2022), P-values for comparison between aggregated results for patients with resistant versus susceptible BSIs

Characteristic	Study level Median [IQR] over all studies	Number of studies reporting item	Patients with resistant BSI Mean over all studies \pm sd	Patients with susceptible BSI Mean over all studies \pm sd	Number of pathogen- specific comparisons included*	P value (χ^2 test)
Mean age	-	-	60.0 \pm 7.6	60.9 \pm 8.9	18	0.764
Median age (years)	-	-	65.5 \pm 8.7	64.1 \pm 12.1	22	0.645
Female sex (%)	57.9 [51.0-63.6]	49	-	-	-	-
Mean Charlson's score	-	-	3.3 \pm 1.3	3.4 \pm 1.6	5	0.867
Median Charlson's score	-	-	3.9 \pm 1.1	3.5 \pm 1.1	13	0.315
Mean APACHEII score	-	-	17.7 \pm 3.1	12.9 \pm 2.7	3	0.111
Patients with any vascular device	-	-	62.9 \pm 25.4	48.3 \pm 25.3	23	0.236
Diabetes mellitus (%)	21.6 [15.3-28.0]	35	24.9 \pm 9.4	22.6 \pm 10.1	28	0.288
COPD (%)	14.4 [10.5-17.6]	26	14.9 \pm 8.4	12.1 \pm 5.9	20	0.241
Liver cirrhosis (%)	7.0 [4.9-11.4]	29	8.9 \pm 6.0	7.4 \pm 6.3	23	0.236
Chronic kidney disease (%)	17.1 [12.1-24.7]	32	22.2 \pm 13.5	15.7 \pm 9.7	28	0.237
Solid malignancy (%)	22.8 [19.7-24.6]	16	20.2 \pm 11.4	21.5 \pm 13.8	13	0.233
Hemato-oncological malignancy (%)	15.6 [9.7-37.5]	17	34.2 \pm 33.1	25.5 \pm 33.5	15	0.083
Intra-venous drug users (%)	5.4 [5.0-5.6]	6	3.5 \pm 2.5	4.8 \pm 1.8	6	0.224
Frail (%)	11.7 [8.2-15.8]	5	16.1 \pm 23.2	13.4 \pm 21.2	5	0.220
Injured (%)	8.1 [5.3-9.6]	4	5.2 \pm 7.5	5.2 \pm 3.7	3	0.199

BSI, bloodstream infection; sd, standard deviation

* Some studies included multiple comparisons, due to including different pathogens, endpoints, or comparator groups.

Study level information was not reported for the following preselected patient categories: obese patients, pregnant women, patients with COVID-19 and patients with elective surgeries.

Table S4: Sources of bloodstream infections in drug-resistant and drug-susceptible bloodstream infections for six key pathogens

Table S4 Mean percentages of the different bloodstream infection sources over all comparisons (N=, from 56 studies) of the excess health risk of patients with drug-resistant bloodstream infections for six key pathogens. All patients with bloodstream infections were included.

Source of bloodstream infection (BSI)	Mean \pm standard deviation	Number of pathogen-specific comparisons#
Primary BSI* (%)	31.7 \pm 2.4	8
Catheter related (%)	21.1 \pm 16.2	26
Urinary tract (%)	35.3 \pm 78.2	25
Respiratory tract (%)	15.6 \pm 12.8	23
Gastrointestinal tract (%)	24.1 \pm 29.9	21
Skin and soft tissue (%)	9.2 \pm 6.8	16
Surgical site (%)	3.8 \pm 2.7	7

* In some studies catheter-related BSIs were categorized as primary BSI

Including comparisons to susceptible infection or uninfected patients