

Supplementary tables for:

Exploring the potential influence of human gut microbiota on gut resistome: A systematic review.

Table S1. PRISMA Checklist

Table S2. Table S2: Search algorithms and databases used to source articles for the review.

Table S3. The Joanna Briggs Institute (JBI) critical appraisal checklist for longitudinal studies.

Table S4. The Joanna Briggs Institute (JBI) critical appraisal checklist for Cross-sectional studies.

Table S5. Summary of bioinformatic databases used in the included studies for analysis of metagenomic sequence data

Table S6. Summary of bioinformatic pipelines and tools used in the included studies for analysis of metagenomic sequence data

Table **S7**. Microbiota composition and abundance and *E. coli* resistome, gene product and associated antibiotic resistance in healthy individuals

Table **S8**. *E. coli* resistome profile, associated gene product and antibiotic resistance in healthy individuals.

Table S1: PRISMA Checklist. Adapted from Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D., Shamseer, L., Tetzlaff, J.M., Akl, E.A., Brennan, S.E. and Chou, R., 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *bmj*, 372.

Section and Topic	Item #	Checklist item	Reported on page
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	2-3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when	3

Section and Topic	Item #	Checklist item	Reported on page
		each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Not Applicable
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Not applicable
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Not applicable
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	7,11,14
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Not applicable
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Not applicable
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Not applicable

Section and Topic	Item #	Checklist item	Reported on page
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Not applicable
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Not applicable
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	5,6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	4
Study characteristics	17	Cite each included study and present its characteristics.	Not applicable
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table S3, Table S4
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimates and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Not Applicable
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Not applicable
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Not applicable
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Not applicable
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Not applicable
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Not applicable
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Not applicable
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	14-17
	23b	Discuss any limitations of the evidence included in the review.	17
	23c	Discuss any limitations of the review processes used.	17
	23d	Discuss implications of the results for practice, policy, and future research.	18
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Not applicable

Section and Topic	Item #	Checklist item	Reported on page
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Not applicable
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Not applicable
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	18
Competing interests	26	Declare any competing interests of review authors.	18
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Not applicable

Table S2: Search algorithms and databases used to source articles for the review

Database	Search algorithm
Search category 1	
Web of Science	"Human gut microbiome" OR "human gut microbiota" OR "human gut microflora" OR "human gut bacteria" OR "human intestinal bacteria" AND resistome OR "antibiotic resistance genes" OR ARG
Scopus	"Human gut microbiome" OR "human gut microbiota" OR "human gut microflora" OR "human gut bacteria" OR "human intestinal bacteria" AND resistome OR "antibiotic resistance genes" OR ARG
PubMed	(i) "Human gut microbiome" OR "human gut microbiota" OR "human gut microflora" OR "human gut bacteria" OR "human intestinal bacteria"; # (i) resistome OR "antibiotic resistance genes" OR ARG. Final search keywords, #(i) AND #(ii).
Search category 2	
Web of Science	"Human gut microbiome" OR "human gut microbiota" OR "human gut microflora" OR "human gut bacteria" OR "human intestinal bacteria" AND resistome OR "antibiotic resistance genes" OR "antibiotic resistance" OR "multiple antibiotic resistance" OR "bacteria resistance" OR "multidrug resistance" AND " <i>Escherichia coli</i> " OR " <i>E. coli</i> "
Scopus	"Human gut microbiome" OR "human gut microbiota" OR "human gut microflora" OR "human gut bacteria" OR "human intestinal bacteria" AND resistome OR "antibiotic resistance genes" OR "antibiotic resistance" OR "multiple antibiotic resistance" OR "bacteria resistance" OR "multidrug resistance" AND " <i>Escherichia coli</i> " OR " <i>E. coli</i> "
PubMed	#(i), "Human gut microbiome" OR "human gut microbiota" OR "human gut microflora" OR "human gut bacteria" OR "human intestinal bacteria"; #(ii), resistome OR "antibiotic resistance genes" OR antibiotic resistance OR "multiple antibiotic resistance" OR "bacteria resistance" OR "multidrug resistance"; #(iii), " <i>Escherichia coli</i> " OR " <i>E. coli</i> ". Final search keywords, # iv, #(i) AND #(ii) AND #(iii)

Table S3. The Joanna Briggs Institute (JBI) critical appraisal checklist for longitudinal studies.

Study	Questions											Score %
	1	2	3	4	5	6	7	8	9	10	11	
Bargheet et al., 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	unclear	unclear	Yes	9/11 (81.8%)
Lebeaux et al., 2021.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	unclear	unclear	Yes	9/11 (81.8%)
Pärnänen et al., 2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	unclear	unclear	Yes	9/11(81.8%)
Li et al., 2021.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	unclear	unclear	Yes	9/11 (81.8%)
Zhang et al., 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	unclear	unclear	Yes	9/11(81.8%)

The checklist questions include **1:** Were the two groups similar and recruited from the same population; **2:** Were the exposures measured similarly to assign people to both exposed and unexposed groups? **3:** Was the exposure measured in a valid and reliable way? **4:** Were confounding factors identified? **5:** Were strategies to deal with confounding factors stated? **6:** Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)? **7:** Were the outcomes measured in a valid and reliable way? **8:** Was the follow up time reported and sufficient to be long enough for outcomes to occur? **9:** Was follow up complete, and if not, were the reasons to loss to follow up described and explored? **10:** Were strategies to address incomplete follow up utilized? **11:** Was appropriate statistical analysis used?

Table S4. The Joanna Briggs Institute (JBI) critical appraisal checklist for Cross-sectional studies.

Study	Questions								Score (%)
	1	2	3	4	5	6	7	8	
Pereira-Dias et al., 2021.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8 (100%)
Trinh et al., 2023.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8 (100%)
Wang et al., 2021.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8(100%)
Dwiyanto et al., 2023	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8 (100%)
Clemente et al., 2015.	Yes	Yes	Yes	Yes	Yes	Yes	unclear	Yes	7/8(87.5%)
Khan et al., 2019	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/8(100%)

The checklist questions include: **1.** Were the criteria for inclusion in the sample clearly defined? **2.** 2.

Were the study subjects and the setting described in detail? **3.** Was the exposure measured in a valid and reliable way? **4.** Were objective, standard criteria used for measurement of the condition **5.** Were confounding factors identified **6.** Were strategies to deal with confounding factors stated? **7.** Were the outcomes measured in a valid and reliable way? **8.** Was appropriate statistical analysis used?.

Table S5: Summary of bioinformatic databases used in the included studies for analysis of metagenomic sequence data

Bioinformatic Database	Usage
CARD (Comprehensive Antibiotic Resistance Database)	identifying and annotating antibiotic resistance genes (ARGs)
CHOCOPhlAn	Taxonomic and functional profiling
NCBI GenBank	Filtering out human DNA contaminant sequences and for OTU identification
Human Reference Genome (GRCh38)	Filtering out human genome sequences
NanoARG	Reference database of mobile genetic elements (MGEs)
ResFinder	For identifying acquired or mobile ARGs
SILVA v.123	Reference database for 16S rRNA sequence classification
UniRef-90	Functional profiling in conjunction with HUMAnN

KEGG	To identify and quantify the abundance and coverage of metabolic pathways
VFDB (Virulence Factors Database)	For virulence factors identification
HMP (Human Microbiome Project)	A comparative dataset for control
ARGANNOT	For detecting ARGs
ARDB (Antibiotic Resistance Genes Database)	For the detection and classification of ARGs
NCBI nt and nr	For aligning sequences and identifying homologs
MetaHIT	Reference database to align gut metagenomic sequence against the database catalogue

Table S6. Summary of bioinformatic pipelines and tools used in the included studies for analysis of metagenomic sequence data

Bioinformatic Pipelines and Tools	Usage
MetaPhlAn3	Metagenome profiling and determination of relative abundances of microbial taxa
MetaSPAdes	Assemblage of reads into contigs
Bowtie2	Mapping sequences against the human genome and for resistome annotation
PANDAsseq	Used for merging paired end reads from FASTQ files
Prokka	Predicting open reading frames (ORFs)
CD-HIT	Collapsing redundant ORFs and clustering redundant ARGs
ABRicate	Annotating ORFs by against the CARD database
ShortBRED	Profiling and quantifying ARGs
HUMAnN	Used for profiling metabolic pathways
StrainGST from StrainGE	Performing strain-level analysis and in this case <i>Escherichia coli</i>
PanPhlAn	Strain-level analysis by mapping samples to the pangenome
SAMtools	Used for filtering and counting reads, converting bam to fastq
MetaPhlAn2	Used for taxonomic profiling and species-level community profiling
StrainPhlAn	Strain-level profiling and strain tracking analysis
VSEARCH	clustering, aligning, and analyzing nucleotide sequences, in th is case it was used to remove redundancy in the custom MGE database
SPAdes	metagenomic assembly and metagenome binning
CheckM	For checking/ estimating genome completion and contamination
MetaBAT	Metagenome binning
Prodigal	Gene prediction

MEGAHIT	Metagenome assembly
DIAMOND	Sequence alignment/functional annotation of genes
MetaCherchant	For reconstructing the genomic context of ARG sequences
KneadData	Used to remove adapters, sequencing primers, and decontaminate human reads
BioBakery3	Has comprehensive suite of bioinformatic tools to process metagenomic sequence data
BLASTn and BLASTx	Aligning sequences for comparison to identify homologs

Table S7. Microbiota composition and abundance and *E. coli* resistome, gene product and associated antibiotic resistance in healthy individuals

Participant group	Microbiota composition	<i>E. coli</i> resistome profile	Gene product (s)	Associated antibiotic resistance	Ref.
7-day old	<i>Bifidobacterium breve</i> *	<i>acrA, acrD, acrE,</i>	AcrAB-TolC multidrug efflux pump (AcrA), AcrD, AcrE, and AcrF proteins.	Broad range of antibiotics, including tetracyclines, fluoroquinolones, and chloramphenicol.	[38]
	<i>Bifidobacterium longum</i>	<i>acrF</i>			
	<i>Escherichia coli</i>				
	<i>Bifidobacterium bifidum</i>				
	<i>Klebsiella pneumoniae</i>	<i>ampH</i>	Class C beta-lactamase.	Beta-lactam antibiotics.	
	<i>Vellionella parvula</i>	<i>bacA</i>	Bacitracin efflux pump.	Resistance to bacitracin.	
	<i>Bacteroides dorei</i>	<i>EC.15</i>	AcrAB-TolC efflux pump component.	Multidrug resistance, particularly to beta-lactams, tetracyclines, and fluoroquinolones	
	<i>Klebsiella variicola</i>				
	<i>Bacteroides fragilis</i>	<i>emrA</i>	EmrAB-TolC multidrug efflux pump.	Macrolides, fluoroquinolones, and other hydrophobic antibiotics.	
	<i>Enterococcus faecalis,</i>				
	<i>Staphylococcus epidermis</i>				
	<i>Klebsiella pneumoniae</i>	<i>eptA</i>	Phosphoethanolamine transferase.	Polymyxin	
		<i>evgA</i>	EvgS/EvgA two-component regulatory system	Multidrug resistance,	

gadW, gadX

Acid resistance regulators (GadW and GadX).

Acid stress, which indirectly contributes to the survival of bacteria under antibiotic pressure.

marA

Multiple antibiotic resistance protein

Multidrug resistance

mdtE, mdtF, mdtG, mdtH, mdtO

Multidrug efflux pump components.

Multidrug resistance

ompA

Outer membrane protein A.

Contributes to antibiotic resistance by altering membrane permeability, often in synergy with efflux pumps.

pmrF

Lipid A modification enzyme.

Polymyxins

		<i>tolC</i>	TolC protein (part of the efflux pump)	Multidrug resistance	
		<i>yojL</i>	YojL (periplastic protein)	Bacterial stress response enabling it to withstand damaging effect of antimicrobial peptides.	
6 weeks to 1 year old		<i>EF-Tu</i>	Elongation factor Tu.	Pulvomycin.	[39]
		<i>rpoB</i>	RNA polymerase beta subunit.	Rifampicin.	
		<i>uhpT</i>	Fosfomycin resistance protein (hexose-6-phosphate transport protein).	Fosfomycin.	
		<i>murA</i>	UDP-N-acetylglucosamine enolpyruvyl transferase	Fosfomycin.	
		<i>glpT</i>	Glycerol-3-phosphate transporter.	Fosfomycin	
		<i>folP</i>	Dihydropteroate synthase	Sulfonamides.	
		<i>gyrB</i>	DNA gyrase subunit B	Aminocoumarin, Fluoroquinolones,	
		<i>SoxR</i>	Superoxide response regulator.	multiple antibiotics through the activation of efflux pumps.	
		<i>SoxS</i>	Superoxide response activator protein.	Multidrug antibiotic resistance	
		<i>emrE</i>	Multidrug efflux pump	Multidrug antibiotic resistance	
		<i>acrR</i>	AcrAB-TolC efflux pump repressor.	Multidrug antibiotic resistance	
		<i>marR</i>	Multiple antibiotic resistance repressor.	Multidrug antibiotic resistance.	
		<i>mdfA</i>	Multidrug resistance protein.	Multidrug antibiotic resistance.	
		<i>ompF</i>	Outer membrane protein F.	Beta-lactam antibiotics and tetracyclines.	
		<i>nfSA</i>	Nitroreductase.	Nitrofurantoin.	
≤ 90 years	20 most abundant <i>Bifidobacterium adolescentis</i>	(not exclusive) <i>mdfA</i>	Multidrug efflux pump protein.	Multiple antibiotics, including aminoglycosides, tetracyclines, fluoroquinolones.	[46]

<i>Prevotella copri</i>	<i>emrE</i>	Multidrug efflux pump protein.	Small hydrophobic molecules, including antiseptics, disinfectants, and some antibiotics such as fluoroquinolones.
<i>Bifidobacterium longum</i>			
<i>Collinsella aerofaciens</i>			
<i>Bifidobacterium bifidum</i>			
<i>Eubacterium rectale</i>			
<i>Ruminococcus bromii</i>	<i>ampC</i>	Beta-lactamase enzyme.	Beta-lactam antibiotics.
<i>Escherichia coli</i>			
<i>Bifidobacterium pseudocatenulatum</i>			
<i>Lactobacillus ruminis</i>			
<i>Faecalibacterium prausnitzii</i>			
<i>Blautia obeum</i>			
<i>Bacteroides vulgatus</i>			
<i>Bacteroides uniformis</i>			
<i>Fusicatenibacter saccharivorans</i>			
<i>Roseburia faecis</i>			
<i>Dorea longicatena</i>			
<i>Alistipes putredinis</i>			
<i>Blautia wexlerae</i>			
<i>Eubacterium hallii</i>			

4-50 years	Functional <i>E. coli</i> ARG detection		[47]
<i>Prevotella*</i>			
<i>Ruminococcus</i>	<i>ampC*</i>	Beta-lactamase enzyme.	Beta-lactam antibiotics.
<i>Clostridaceae</i>			
<i>Bacteroides</i>	<i>mdfA</i>	Multidrug efflux pump protein.	Multiple antibiotics, including aminoglycosides, tetracyclines, fluoroquinolones
<i>Succinovibrio</i>			
<i>Bacteroides</i> S24-7			
<i>Oscillospira</i>			
<i>Phascolarctobacterium</i>	<i>bcr</i>	Bicyclomycin resistance protein.	bicyclomycin,.
<i>Ruminobacter</i>			
<i>Desulfovibrio</i>	<i>mdlB</i>	Multidrug resistance protein MdlB.	multiple drugs out of the cell, although specific antibiotics associated to this gene are not well
<i>Helicobacter</i>			

	<i>Oxalobacter formigenes</i>			defined.
		<i>mdlA</i>	Multidrug resistance protein MdlA.	multidrug resistance by contributing to extrusion.
		SoxS	Superoxide response activator protein.	Activates the expression of genes including genes encoding efflux pumps that expel antibiotics such as fluoroquinolones and tetracyclines from the cell
1 month	<i>Bifidobacterium*</i> <i>Escherichia</i> <i>Lactobacillus</i> <i>Bacteroides</i> <i>Streptococcus</i> <i>Staphylococcus</i> <i>Blautia</i>	<i>E. coli</i> was highest predictor of ARGs abundance		[40]
6 months	<i>Bifidobacterium*</i> <i>Escherichia</i> <i>Blautia</i> <i>Bacteroides</i> <i>Lactobacillus</i> <i>Eubacterium</i> <i>Akkermansia</i> <i>Subdoligranulum</i>	<i>E. coli</i> was highest predictor of ARGs abundance		[40]
1 year to 5 years	Based on highest abundance of ARGs <i>Escherichia coli</i> <i>Citrobacter werkmanii</i> <i>Klebsiella pneumoniae</i> <i>Enterobacter</i>	68 out of 133 unique types of ARGs in Proteobacteria came from <i>E. coli</i>		[41]

himalayensis
Klebsiella oxytoca
Citrobacter sp001037495
Enterobacter cloacae
Bacteroides fragilis
Bacteroides dorei
Faecalibacterium
prausnitzii
Ruminococcus bromii
Bifidobacterium longum
Bifidobacterium breve
Haemophilus
parainfluenzae
Morganella morganii
Faecalicatena gnavus
Tyzzereella nexilis
Blautia wexlerae
Ruminococcus
bicirculans
Flavonifractor plautii
Veillonella seminalis
Erysipelatoclostridium
ramosum
(*Thomasclavelia ramosa*)
Agathobacter rectalis
Staphylococcus
epidermidis
Collinsella sp003487125
Bifidobacterium
pseudocatenulatum
Bacteroides uniformis
Bacteroides ovatus
Bacteroides
thetaiotaomicron

	<i>Parabacteroides distasonis</i> <i>Alistipes putredinis</i> <i>Prevotella buccae</i>			
Non-Pregnant (NP)	Based on 16S metagenomics Lower species diversity in pregnant compared to NP Phylum Bacteroidetes* Firmicutes Proteobacteria Actinobacteria	<i>E. coli</i> was the most prevalent AR species	<i>E. coli</i> isolates were resistant to Kanamycin Gentamicin Metronidazole Oxytetracycline Cycloserine Chloramphenicol Cefixime Trimethoprim/sulfamethoxazole Azithromycin Ampicillin Amoxicillin	[48]
Pregnant 1st-Trim (P1)	Firmicutes* Bacteroidetes Proteobacteria Actinobacteria			
Pregnant 3 rd -Trim (P3)	Firmicutes* Bacteroidetes Actinobacteria Proteobacteria			

*Most abundant; AST; NP= non-pregnant.

Table S8. *E. coli* resistome profile, associated gene product and antibiotic resistance in healthy individuals

Associated resistance group	<i>E. coli</i> resistome profile	Gene product (s)	Associated antibiotic resistance
MDR-Efflux pump system	<i>acrA, acrD, acrE, acrF,</i>	AcrAB-TolC multidrug efflux pump (AcrA), AcrD, AcrE, and AcrF proteins.	Broad range of antibiotics, including tetracyclines, fluoroquinolones, and chloramphenicol.
	<i>acrR</i>	AcrAB-TolC efflux pump repressor.	Multidrug antibiotic resistance
	<i>mdtE, mdtF, mdtG, mdtH, mdtO</i>	Multidrug efflux pump components.	Multidrug resistance
	<i>mdfA</i>	Multidrug resistance protein.	Multidrug antibiotic resistance.
	<i>emrA</i>	EmrAB-TolC multidrug efflux pump.	Macrolides, fluoroquinolones, and other hydrophobic antibiotics.
	<i>emrE</i>	Multidrug efflux pump	Multidrug antibiotic resistance
	<i>marA</i>	Multiple antibiotic resistance protein	Multidrug resistance
	<i>marR</i>	Multiple antibiotic resistance repressor.	Multidrug antibiotic resistance.
	<i>SoxR</i>	Superoxide response regulator.	multiple antibiotics through the activation of efflux pumps.
	<i>SoxS</i>	Superoxide response activator protein.	Multidrug antibiotic resistance
	<i>gadW, gadX</i>	Acid resistance regulators (GadW and GadX).	Acid stress, which indirectly contributes to the survival of bacteria under antibiotic pressure.
	<i>tolC</i>	TolC protein (part of the efflux pump)	Multidrug resistance
Aminocoumarin, Fluoroquinolones	<i>gyrB</i>	DNA gyrase subunit B	Aminocoumarin, Fluoroquinolones
Polypeptides	<i>eptA</i>	Phosphoethanolamine transferase.	Polymyxin
	<i>bacA</i>	Bacitracin efflux pump.	Resistance to bacitracin.
	<i>pmrF</i>	Lipid A modification enzyme.	
Multidrug resistance	<i>evgA</i>	EvgS/EvgA two-component regulatory system	

	<i>EC.15</i>	AcrAB-TolC efflux pump component. protein F.	Multidrug resistance, particularly to beta-lactams, tetracyclines, and fluoroquinolones
Folate pathway inhibitor	<i>folP</i>	Dihydropteroate synthase	Sulfonamides.
Fosfomycins	<i>murA</i>	UDP-N-acetylglucosamine enolpyruvyl transferase	
	<i>uhpT</i>	Fosfomycin resistance protein (hexose-6-phosphate transport protein).	Fosfomycin.
	<i>glpT</i>	Glycerol-3-phosphate transporter.	Fosfomycin
Nitrofurans	<i>nfSA</i>	Nitroreductase.	
Betalactams	<i>ompA</i>	Outer membrane protein A.	Contributes to antibiotic resistance by altering membrane permeability, often in synergy with efflux pumps.
	<i>ampC</i>	Beta-lactamase enzyme.	Beta-lactam antibiotics.
	<i>ompF</i>	Outer membrane	Beta-lactam antibiotics and tetracyclines.
	<i>EC.15</i>	AcrAB-TolC efflux pump component. protein F.	Multidrug resistance, particularly to beta-lactams, tetracyclines, and fluoroquinolones
Peptides	<i>yojL</i>	YojL (periplastic protein)	Bacterial stress response enabling it to withstand damaging effect of antimicrobial peptides.

Eligible studies used for the review

1. Bargheet, A.; Klingenberg, C.; Esaiassen, E.; Hjerde, E.; Cavanagh, J.P.; Bengtsson-Palme, J.; Pettersen, V.K. Development of early life gut resistome and mobilome across gestational ages and microbiota-modifying treatments. *EBioMedicine* **2023**, *92*, 104606.
2. Lebeaux, R.M.; Coker, M.O.; Dade, E.F.; Palys, T.J.; Morrison, H.G.; Ross, B.D.; Baker, E.R.; Karagas, M.R.; Madan, J.C.; Hoen, A.G. The infant gut resistome is associated with *E. coli* and early-life exposures. *BMC Microbiol.* **2021**, *21*, 201.
3. Pärnänen, K.; Karkman, A.; Hultman, J.; Lyra, C.; Bengtsson-Palme, J.; Larsson, D.J.; Rautava, S.; Isolauri, E.; Salminen, S.; Kumar, H.; Satokari, R. Maternal gut and breast milk microbiota affect infant gut antibiotic resistome and mobile genetic elements. *Nat. commun.* **2018**, *9*, 3891.
4. Li, X.; Stokholm, J.; Brejnrod, A.; Vestergaard, G.A.; Russel, J.; Trivedi, U.; Thorsen, J.; Gupta, S.; Hjelmsø, M.H.; Shah, S.A.; Rasmussen, M.A. The infant gut resistome associates with *E. coli*, environmental exposures, gut microbiome maturity, and asthma-associated bacterial composition. *Cell Host & Microbe* **2021**, *29*, 975-987.
5. Zhang, W.; Han, N.; Zhang, T.; Qiang, Y.; Peng, X.; Li, X.; Kan, B. The spatial features and temporal changes in the gut microbiota of a healthy Chinese population. *Microbiol. Spectr.* **2022**, *10*, pp.e01310-22.
6. Pereira-Dias, J.; Nguyen Ngoc Minh, C.; Tran Thi Hong, C.; Nguyen Thi Nguyen, T.; Ha Thanh, T.; Zellmer, C.; Chung The, H.; Pike, L.; Higginson, E.E.; Baker, S. The gut microbiome of healthy Vietnamese adults and children is a major reservoir for resistance genes against critical antimicrobials. *J. Infect. Dis.* **2021**, *224*(Supplement_7), S840-S847.
7. Trinh, P.; Roberts, M.C.; Rabinowitz, P.M.; Willis, A.D. Differences in gut metagenomes between dairy workers and community controls: a cross-sectional study. *bioRxiv.* **2023** (Preprint)
8. Wang, Y.; Lyu, N.; Liu, F.; Liu, W.J.; Bi, Y.; Zhang, Z.; Ma, S.; Cao, J.; Song, X.; Wang, A.; Zhang, G. More diversified antibiotic resistance genes in chickens and workers of the live poultry markets. *Environ. Int.* **2021**, *153*, 106534.
9. Dwiyanto, J.; Huët, M.A.L.; Hussain, M.H.; Su, T.T.; Tan, J.B.L.; Toh, K.Y.; Lee, J.W.J.; Rahman, S.; Chong, C.W. Social demographics determinants for resistome and microbiome variation of a multiethnic community in Southern Malaysia. *npj Biofilms and Microbiomes* **2023**, *9*, 55.
10. Clemente, J.C.; Pehrsson, E.C.; Blaser, M.J.; Sandhu, K.; Gao, Z.; Wang, B.; Magris, M.; Hidalgo, G.; Contreras, M.; Noya-Alarcón, Ó.; Lander, O. The microbiome of uncontacted Amerindians. *Sci. Adv.* **2015**, *1*, e1500183.
11. Khan, I.; Yasir, M.; Farman, M.; Kumosani, T.; AlBasri, S.F.; Bajouh, O.S.; Azhar, E.I. Evaluation of gut bacterial community composition and antimicrobial resistome in pregnant and non-pregnant women from Saudi population. *Infect. Drug Resist.* **2019**, *12*, 1749-1761.

