AMRDETECTOOL
Detection in 30 min

Market analysis and opportunities

NG Biotech

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NG Biotech

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EIT Health is supported by the EIT, a body of the European Union

AMR DETECTOOL DEVICES

AMR DetecTool tests

DetecTool of commercialized tests

- CARBA-5 (NDM, IMP, VIM, OXA-48, KPC)
- CTX-M MULTI (Group 1,2,8,9,25)

DetecTool prototypes

- VAN A/B (VanA, VanB)
- ACINETO (OXA-23)
- C3G (CTX-M MULTI + 3GC activity line)

MARKET ANALYSIS AND OPPORTUNITIES

Detection in 30 min

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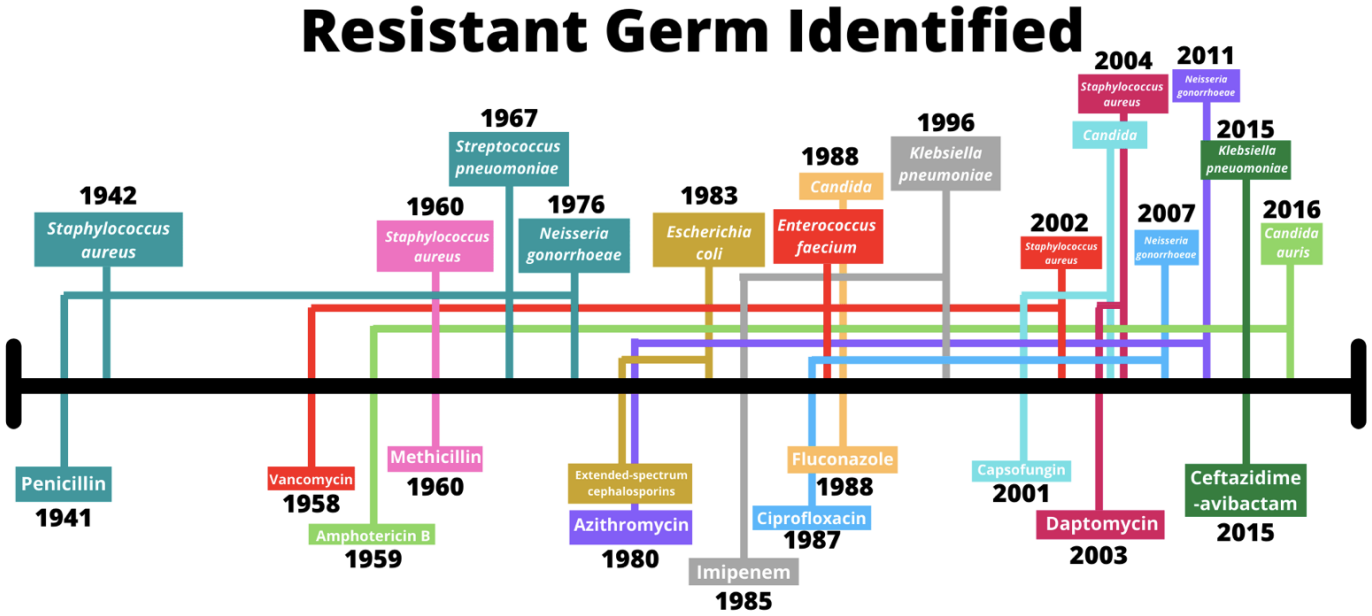
MARKET ANALYSIS

MARKET ANALYSIS AND OPPORTUNITIES



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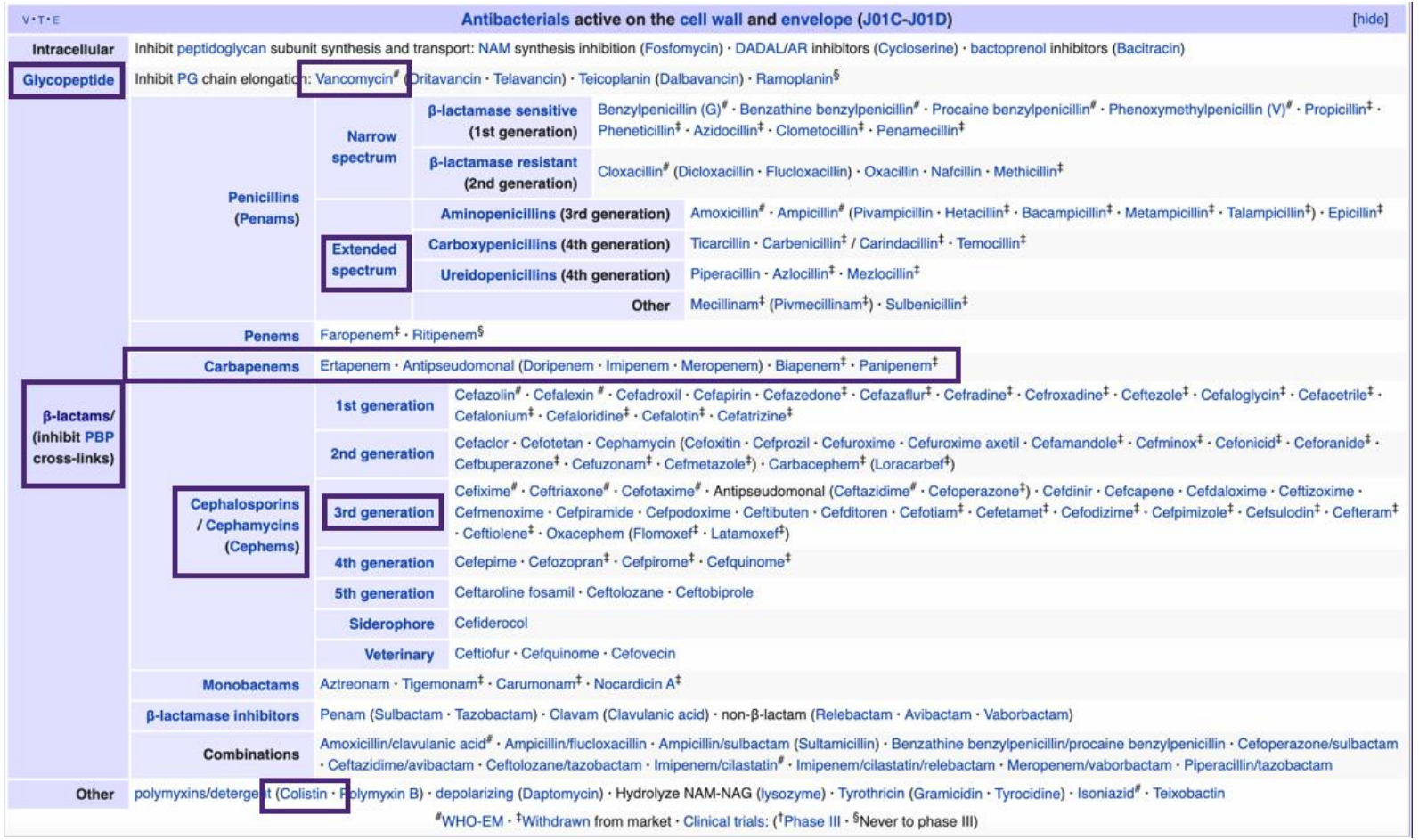

V·T·E

Antibacterials active on the cell wall and envelope (J01C-J01D) [hide]

Intracellular	Inhibit peptidoglycan subunit synthesis and transport: NAM synthesis inhibition (Fosfomycin) · DADAL/AR inhibitors (Cycloserine) · bactoprenol inhibitors (Bacitracin)		
Glycopeptide	Inhibit PG chain elongation: Vancomycin# (Oritavancin · Telavancin) · Teicoplanin (Dalbavancin) · Ramoplanin§		
β-lactams/ (inhibit PBP cross-links)	**Penicillins (Penams)**	**Narrow spectrum**	**β-lactamase sensitive (1st generation)**	Benzylpenicillin (G)# · Benzathine benzylpenicillin# · Procaine benzylpenicillin# · Phenoxymethylpenicillin (V)# · Propicillin‡ · Pheneticillin‡ · Azidocillin‡ · Clometocillin‡ · Penamecillin‡
			β-lactamase resistant (2nd generation)	Cloxacillin# (Dicloxacillin · Flucloxacillin) · Oxacillin · Nafcillin · Methicillin‡
		Extended spectrum	**Aminopenicillins (3rd generation)**	Amoxicillin# · Ampicillin# (Pivampicillin · Hetacillin‡ · Bacampicillin‡ · Metampicillin‡ · Talampicillin‡) · Epicillin‡
			Carboxypenicillins (4th generation)	Ticarcillin · Carbenicillin‡ / Carindacillin‡ · Temocillin‡
			Ureidopenicillins (4th generation)	Piperacillin · Azlocillin‡ · Mezlocillin‡
			Other	Mecillinam‡ (Pivmecillinam‡) · Sulbenicillin‡
	Penems	Faropenem‡ · Ritipenem§		
	Carbapenems	Ertapenem · Antipseudomonal (Doripenem · Imipenem · Meropenem) · Biapenem‡ · Panipenem‡		
	Cephalosporins / Cephamycins (Cephems)	**1st generation**	Cefazolin# · Cefalexin # · Cefadroxil · Cefapirin · Cefazedone‡ · Cefazaflur‡ · Cefradine‡ · Cefroxadine‡ · Ceftezole‡ · Cefaloglycin‡ · Cefacetrile‡ · Cefalonium‡ · Cefaloridine‡ · Cefalotin‡ · Cefatrizine‡	
		2nd generation	Cefaclor · Cefotetan · Cephamycin (Cefoxitin · Cefprozil · Cefuroxime · Cefuroxime axetil · Cefamandole‡ · Cefminox‡ · Cefonicid‡ · Ceforanide‡ · Cefbuperazone‡ · Cefuzonam‡ · Cefmetazole‡) · Carbacephem‡ (Loracarbef‡)	
		3rd generation	Cefixime# · Ceftriaxone# · Cefotaxime# · Antipseudomonal (Ceftazidime# · Cefoperazone‡) · Cefdinir · Cefcapene · Cefdaloxime · Ceftizoxime · Cefmenoxime · Cefpiramide · Cefpodoxime · Ceftibuten · Cefditoren · Cefotiam‡ · Cefetamet‡ · Cefodizime‡ · Cefpimizole‡ · Cefsulodin‡ · Cefteram‡ · Ceftiolene‡ · Oxacephem (Flomoxef‡ · Latamoxef‡)	
		4th generation	Cefepime · Cefozopran‡ · Cefpirome‡ · Cefquinome‡	
		5th generation	Ceftaroline fosamil · Ceftolozane · Ceftobiprole	
		Siderophore	Cefiderocol	
		Veterinary	Ceftiofur · Cefquinome · Cefovecin	
	Monobactams	Aztreonam · Tigemonam‡ · Carumonam‡ · Nocardicin A‡		
	β-lactamase inhibitors	Penam (Sulbactam · Tazobactam) · Clavam (Clavulanic acid) · non-β-lactam (Relebactam · Avibactam · Vaborbactam)		
	Combinations	Amoxicillin/clavulanic acid# · Ampicillin/flucloxacillin · Ampicillin/sulbactam (Sultamicillin) · Benzathine benzylpenicillin/procaine benzylpenicillin · Cefoperazone/sulbactam · Ceftazidime/avibactam · Ceftolozane/tazobactam · Imipenem/cilastatin# · Imipenem/cilastatin/relebactam · Meropenem/vaborbactam · Piperacillin/tazobactam		
Other	polymyxins/detergent (Colistin · Polymyxin B) · depolarizing (Daptomycin) · Hydrolyze NAM-NAG (lysozyme) · Tyrothricin (Gramicidin · Tyrocidine) · Isoniazid# · Teixobactin			

#WHO-EM · ‡Withdrawn from market · Clinical trials: (†Phase III · §Never to phase III)

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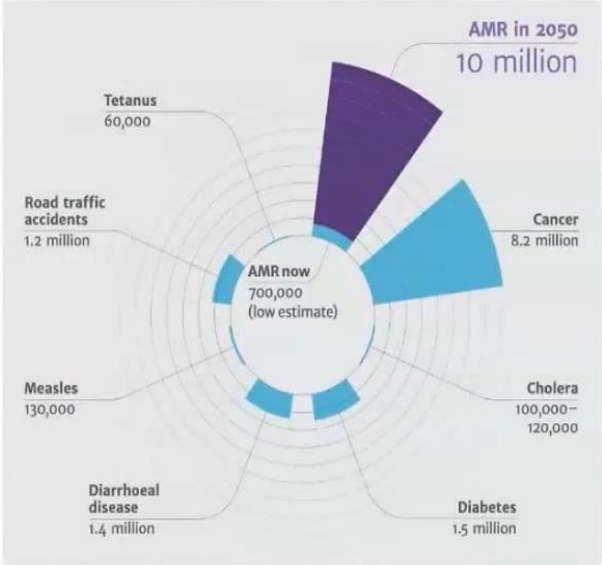
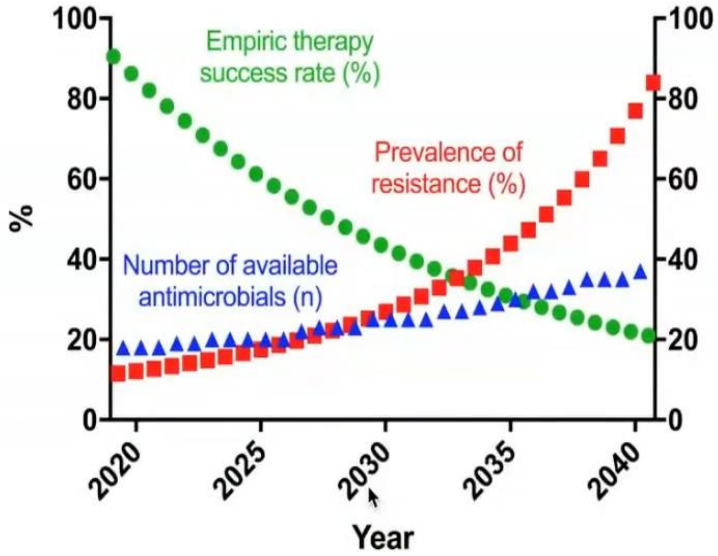
The importance of rapid antimicrobial susceptibility testing (AST)



Sir O'Neill, Review on Antimicrobial Resistance 2014



Smith & Kirby Clin Lab Med. 2019

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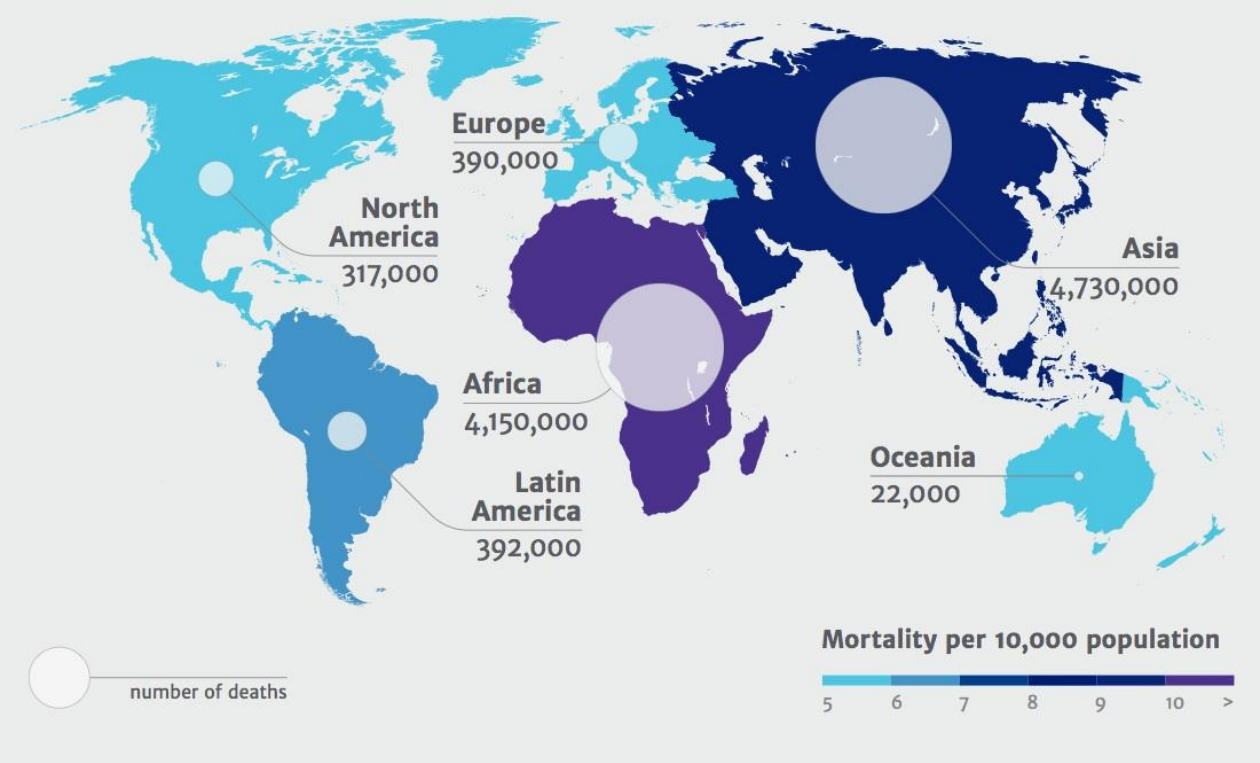
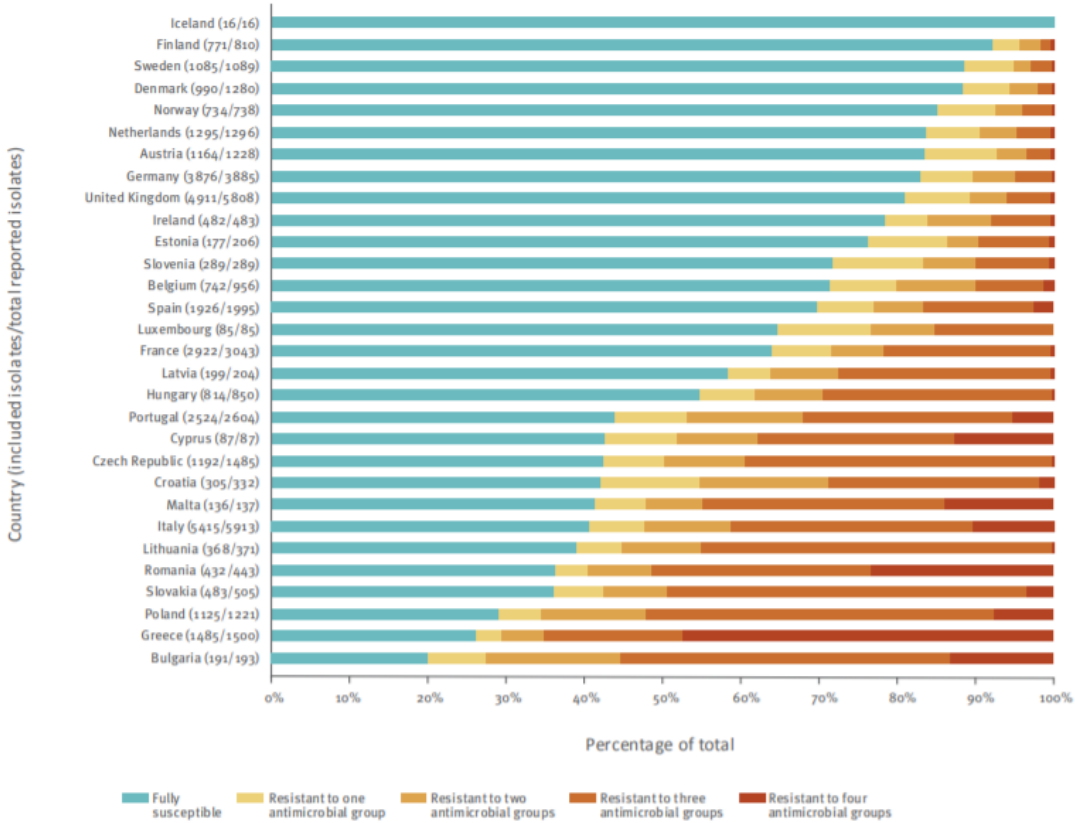


Without action, by 2050 someone could die every three seconds as a result of AMR, says the Review on Antimicrobial Resistance. That's 10 million people a year.

MARKET ANALYSIS AND OPPORTUNITIES

Figure 3.7. *Klebsiella pneumoniae*. Distribution of isolates: fully susceptible and resistant to one, two, three and four antimicrobial groups (among isolates tested against fluoroquinolones, third-generation cephalosporins, aminoglycosides and carbapenems), EU/EEA countries, 2018



Only data from isolates tested against all included antimicrobial groups are included in analysis.

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Figure 3.5. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2018

Figure 3.11. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2018

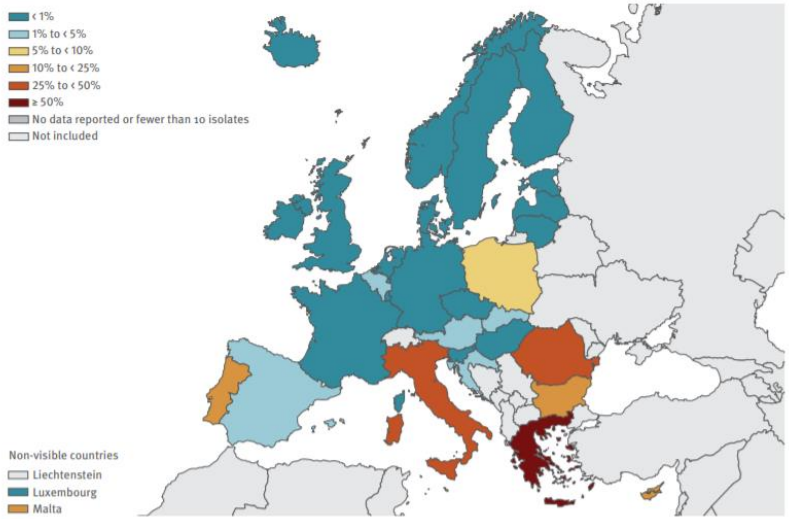

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Figure 3.3. *Escherichia coli*. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2018

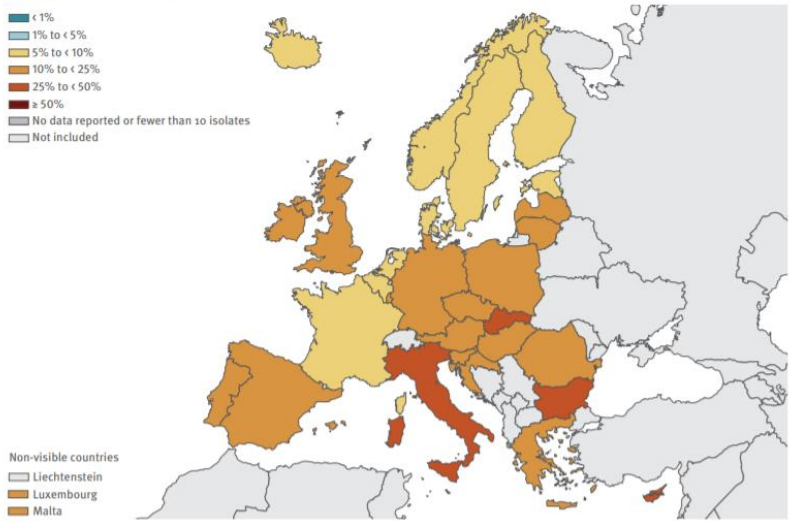

Figure 3.9. *Klebsiella pneumoniae*. Percentage (%) of invasive isolates with resistance to third-generation cephalosporins, by country, EU/EEA countries, 2018

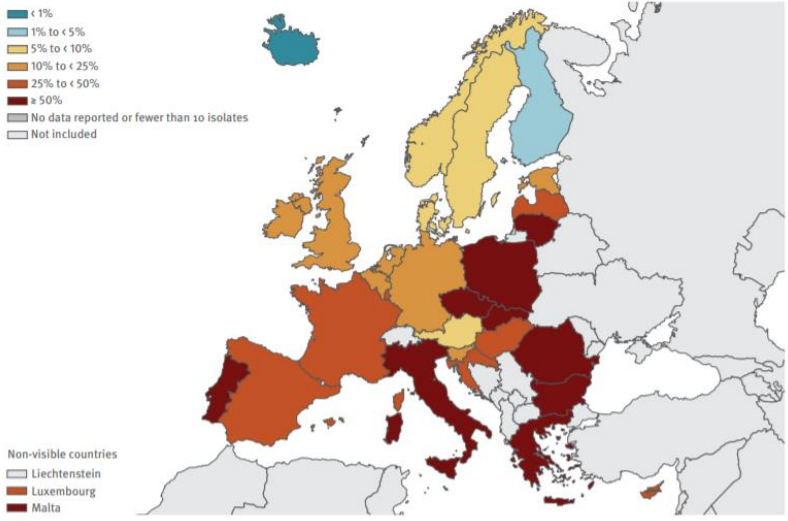

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Figure 3.22. *Acinetobacter* spp. Percentage (%) of invasive isolates with resistance to carbapenems, by country, EU/EEA countries, 2018

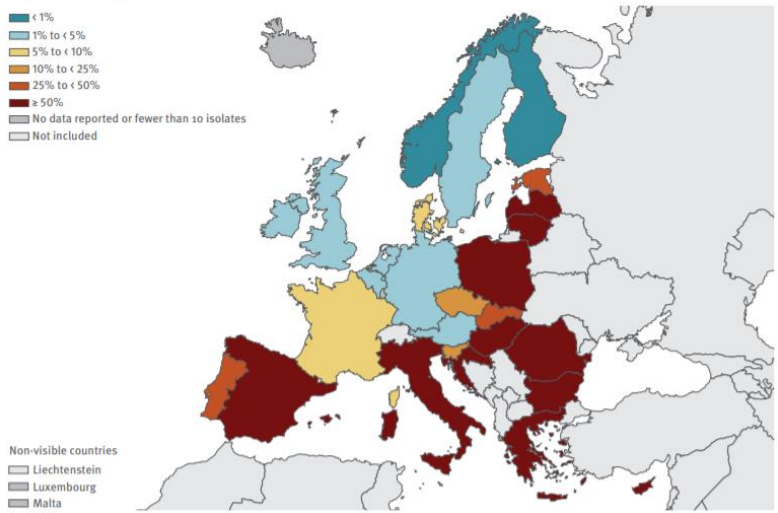
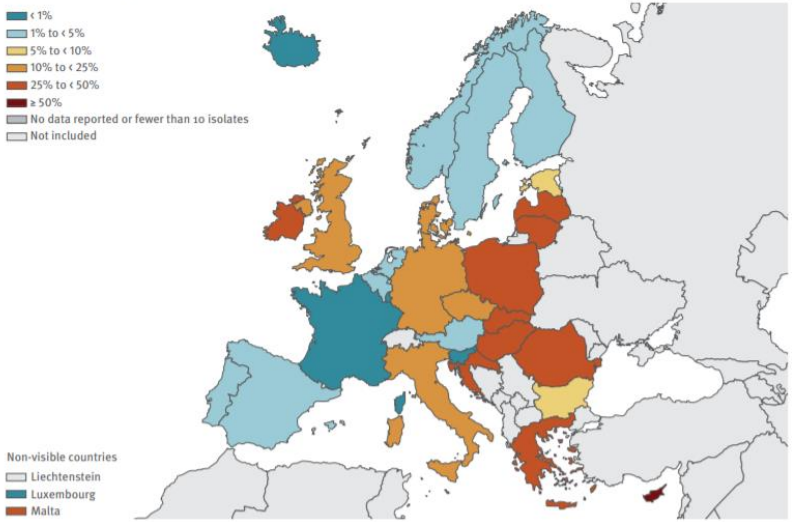


Figure 3.27. *Enterococcus faecium*. Percentage (%) of invasive isolates with resistance to vancomycin, by country, EU/EEA countries, 2018



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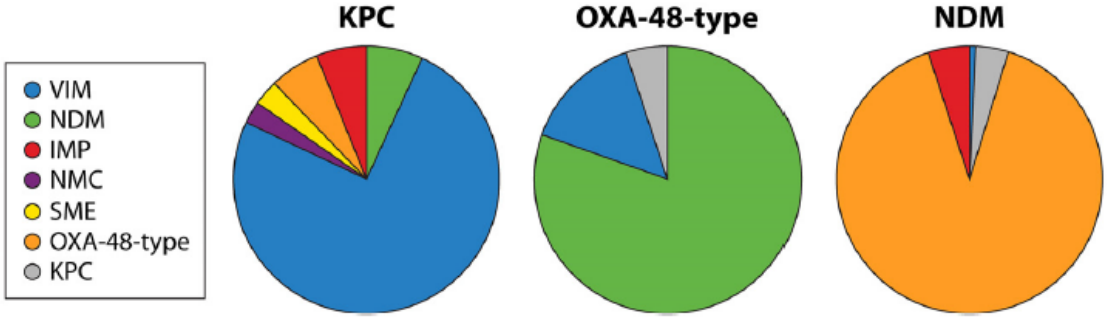

FIG 6 Coproduction of carbapenemases in the same organism. Data for production of KPC β-lactamases, OXA-48-type β-lactamases, and NDM β-lactamases with other carbapenemases were compiled from Table 2.

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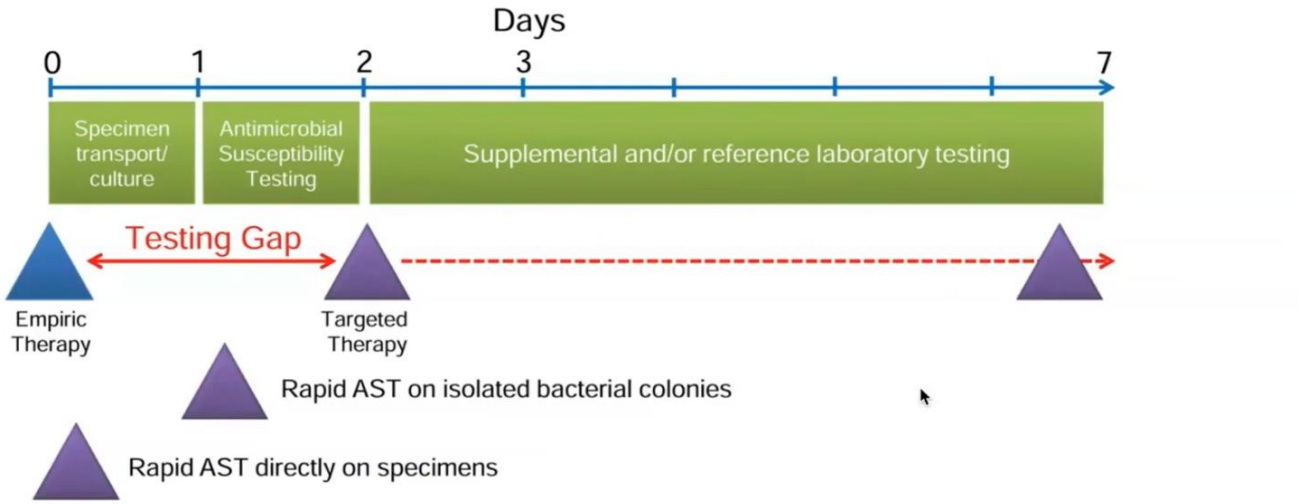
Where to use the DetecTool

Rapid from when?



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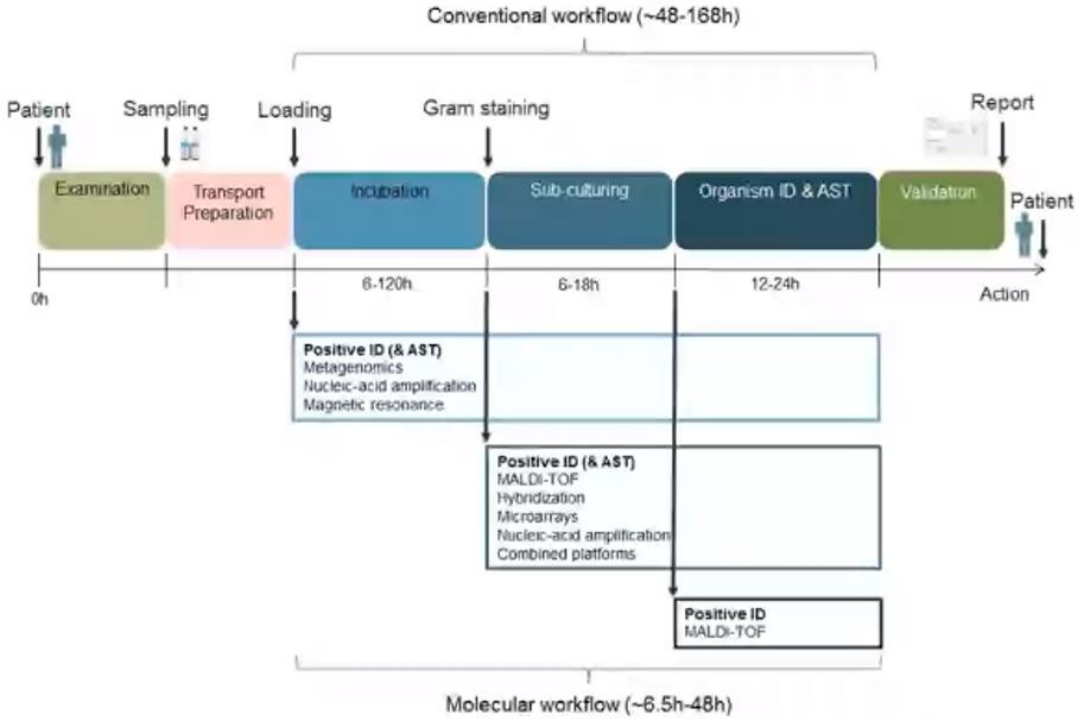
Diagnosis of bloodstream infections from positive blood cultures and directly from blood samples: recent developments in molecular approaches



Peker N et al. Clin Microbiol Infect 2018;24(9):944-955.

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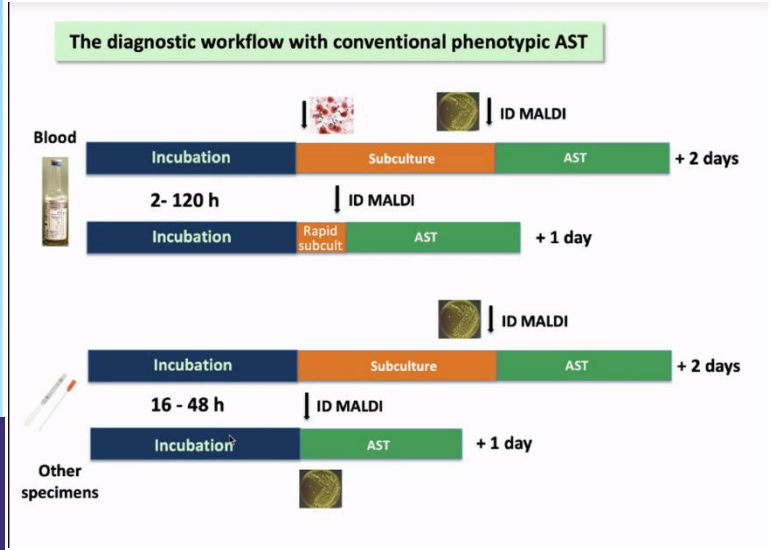
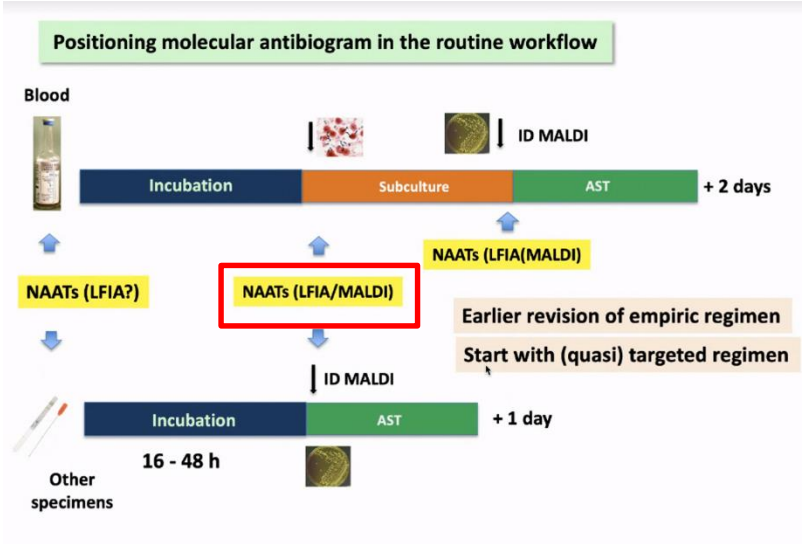
From **bacterial culture**

From **direct sample**





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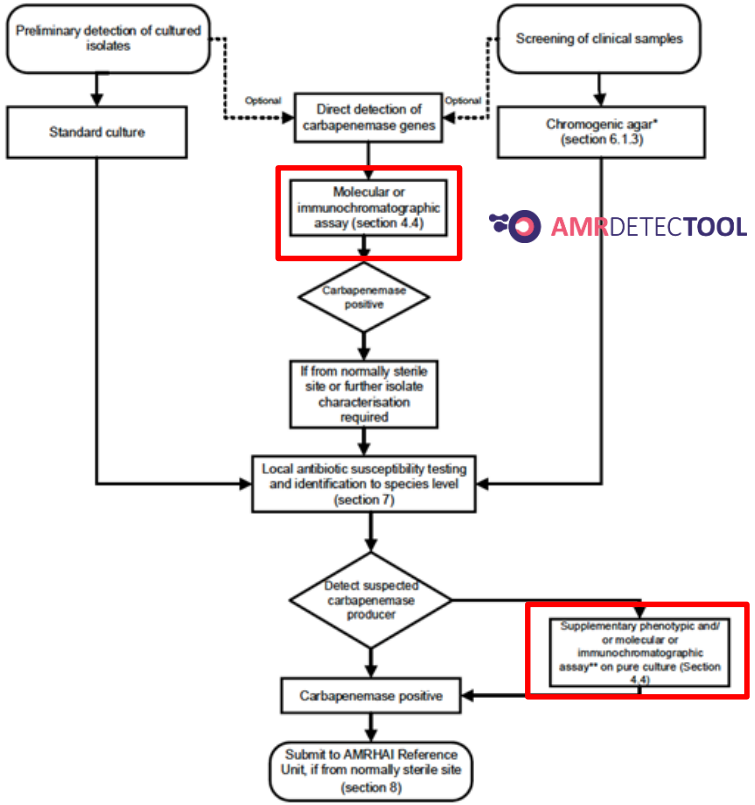
Appendix 1: Flowchart for the detection of carbapenemases on cultured isolates and screening samples



UK Standards for Microbiology Investigations

Detection of bacteria with carbapenem-hydrolysing β-lactamases (carbapenemases)

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Molecular antibiogram?

Detecting resistance mechanisms at the molecular level (genes, proteins)

↘

Using the information as a proxy for antimicrobial susceptibility profiling

↘

Translating to clinical decision

Arena *et al* – Fut Microbiol, 2017

MARKET ANALYSIS AND OPPORTUNITIES

Klebsiella pneumoniae

Molecular antibiogram:

CTX-M	not detected
KPC	DETECTED
VIM	not detected
OXA-48	not detected
NDM	not detected
IMP	not detected
MCR-1	not detected

- Presumed resistance to all older beta-lactams including carbapenems
- Presumed susceptibility to anti-KPC agents (CAZ/AVI, MER/VBR, IMI/RLB, CFDC)
- No relevant info about other agents
- No MIC values

Coverage of Carbapenemase-Producing *Enterobacterales* (CPE) by the new beta-lactamase inhibitor combinations and new beta-lactams

R-mechanism	CAZ/AVI	MER/VAB	IMI/REL	CFDC	*ATM/AVI*
KPC	+	+	+	+	+
OXA-48	+	-	-	+	+
VIM	-	-	-	+	+
NDM	-	-	-	+	+
IMP	-	-	-	+	+

CAZ/AVI = ceftazidime/avibactam
MER/VAB = meropenem/vaborbactam
IMI/REL = imipenem/relebactam
CFDC = cefiderocol
ATM/AVI = aztreonam/avibactam

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Molecular vs. conventional antibiogram: different information

Antibiotic	MIC mg/L (S/I/R)
Amoxi/Clav	>16 R
Pip/Tazo	>128 R
Ceftriaxone	>4 R
Ceftazidime	>128 R
Cefepime	>32 R
Ertapenem	>1 R
Imipenem	>16 R
Meropenem	>64 R
Fosfomycin	32 S
Amikacin	>16 R
Gentamicin	1 S
Ciprofloxacin	>4 R
Tygecycline	0.5
Colistin	>8 R
CAZ/AVI	4 S
MER/VBR	0.5 S

Conventional antibiogram

Klebsiella pneumoniae

Molecular antibiogram:

CTX-M	not detected
KPC	DETECTED
VIM	not detected
OXA-48	not detected
NDM	not detected
IMP	not detected
MCR-1	not detected

- Presumed resistance to all older beta-lactams including carbapenems
- Presumed susceptibility to anti-KPC agents (CAZ/AVI, MER/VBR, IMI/RLB, CFDC)
- No relevant info about other agents
- No MIC values

Antibiotic	status
Amoxi/Clav	(R)
Pip/Tazo	(R)
Ceftriaxone	(R)
Ceftazidime	(R)
Cefepime	(R)
Ertapenem	(R)
Imipenem	(R)
Meropenem	(R)
Fosfomycin	?
Amikacin	?
Gentamicin	?
Ciprofloxacin	?
Tygecycline	?
Colistin	?
CAZ/AVI	(S)
MER/VBR	(S)
IMI/RLB	(S)
CFDC	(S)

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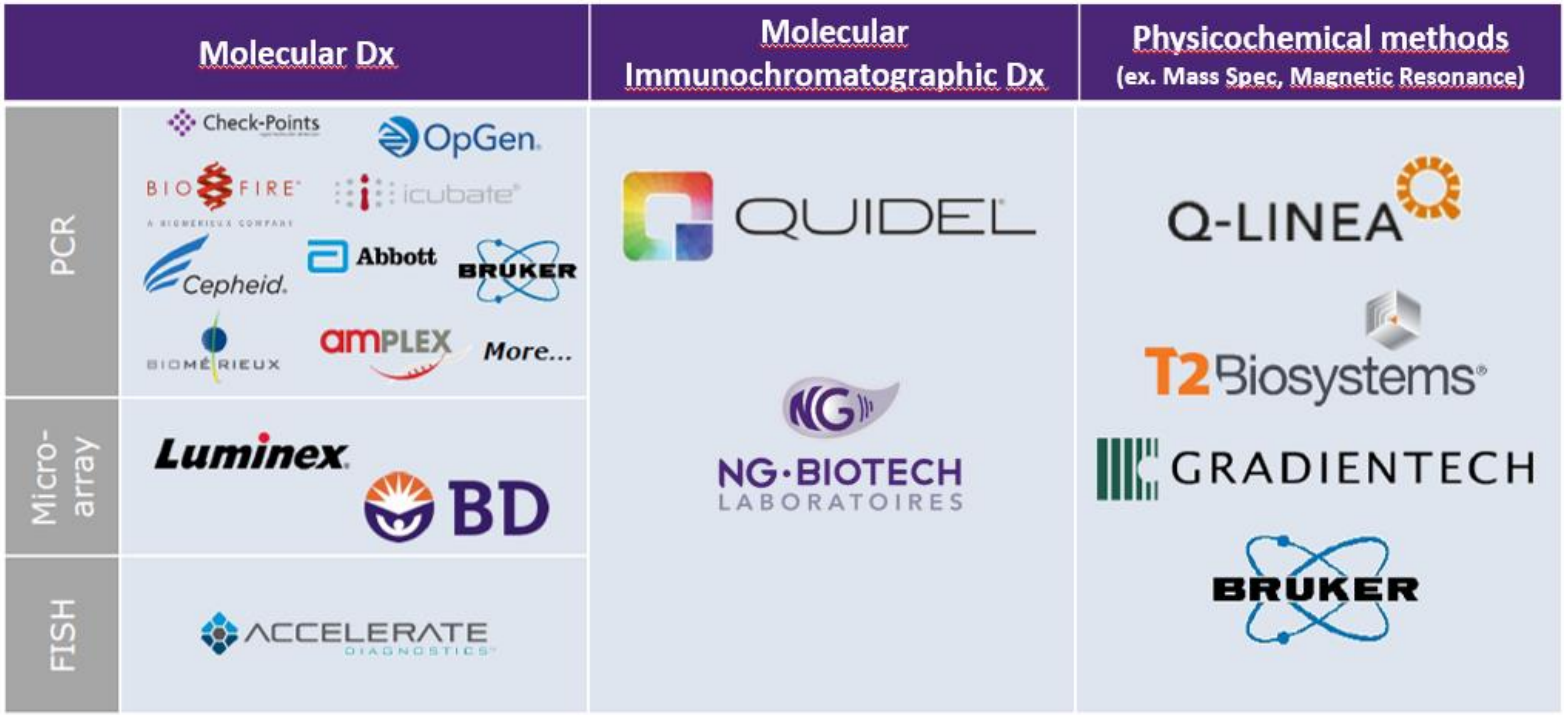
Market opportunities

PCR- based tests dominate the infectious medical device landscape



MARKET ANALYSIS AND OPPORTUNITIES

Existing technologies that do not require isolated colonies

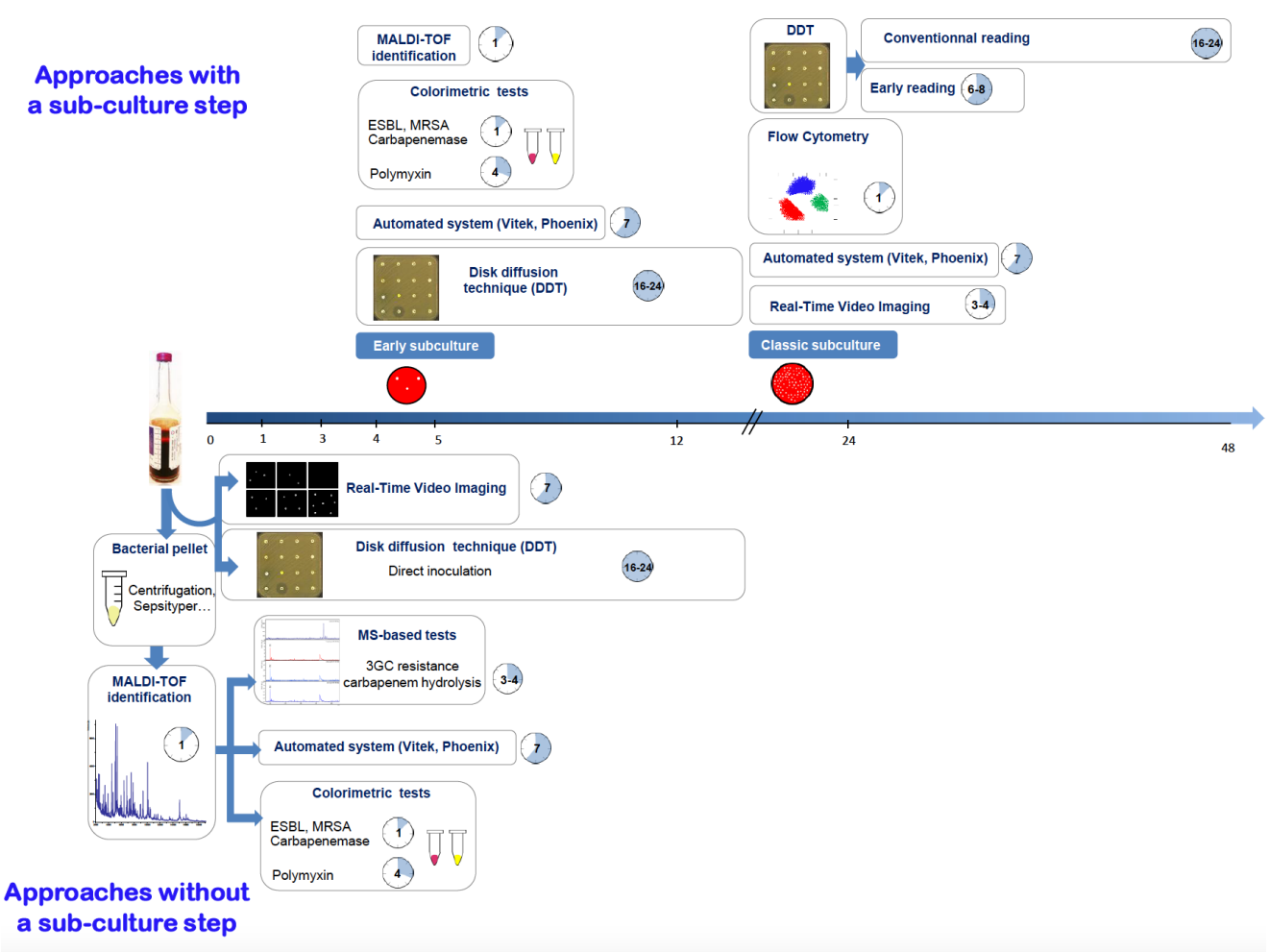
Pros

- Same day results.
- High accuracy with detection of specific carbapenemase gene.
- CLSI endorsed.

Cons

- Low accessibility to those technologies.
- Good accessibility but only detecting the activity.

MARKET ANALYSIS AND OPPORTUNITIES



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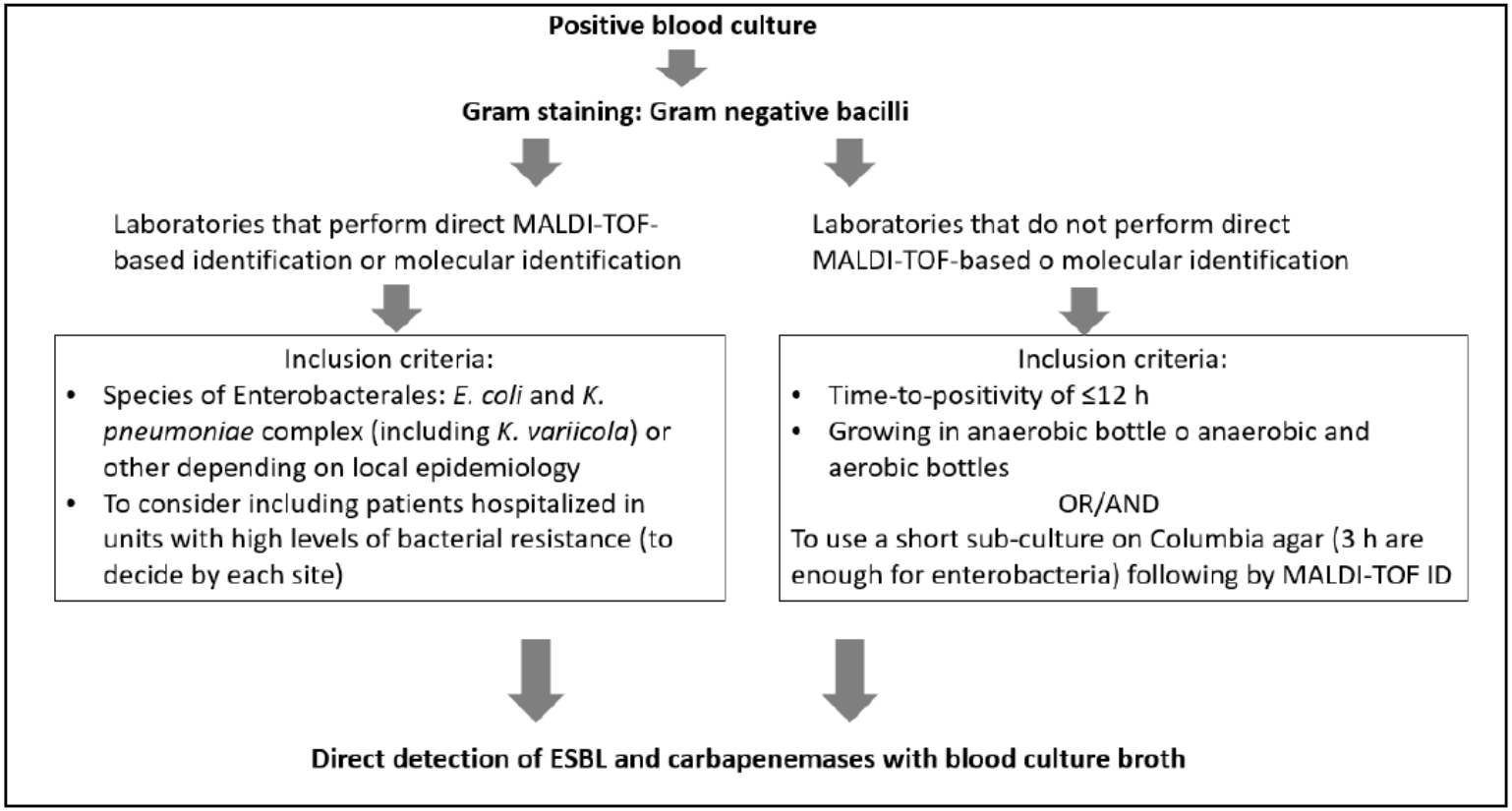
ESBL (CARBA) detection in blood culture



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Detection in 30 min

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ESBL (CARBA) detection in urine

Samples from patients with suspicion of urosepsis and/or pyelonephritis:

- Direct clinician request or
- Urine and blood culture samples received the same day in lab

↓

Screening for positive urine samples

↓

Laboratories with Flow cytometry:

- Bacterial count ≥5000 bacteria/µL
- Presence of only morphotype of Gram negative bacilli in scatergram

Laboratories without Flow cytometry:

- Reactive strip or sediment parameters of infection (to determine by each laboratory)
- Gram staining positive for Gram negative bacilli*

Laboratories that could perform direct MALDI-TOF-based identification or molecular identification could perform ESBL and carbapenemase detection only with *E. coli* and *K. pneumoniae* complex (including *K.variicola*)

Laboratories could not perform direct MALDI-TOF-based identification will apply the test to all samples with GNB detected Short incubation of selected urines (3 h) followed by MALDI-TOF ID could be another way (with or without previous screening)

↓

Direct detection of ESBL and carbapenemases with direct urine sample

MARKET ANALYSIS AND OPPORTUNITIES

Detection in 30 min

Direct from rectal swabs for screening

For pre-enrichment step, before performing the test:

- Inoculate the rectal swab in 1 mL of transport medium.
- Transfer 400 microliters of this solution to 4 mL of brain heart infusion media supplemented with the following antibiotics (half of a disk, concentration of 30 µg/mL for cefotaxime and 10 µg/mL for ertapenem) and incubate overnight:
  - cefotaxime for the detection of ESBL (when using the NG DetecToolCTXM)
  - ertapenem for the detection of carbapenemases (when using the NG DetecToolCarba-5).

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THANK YOU
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