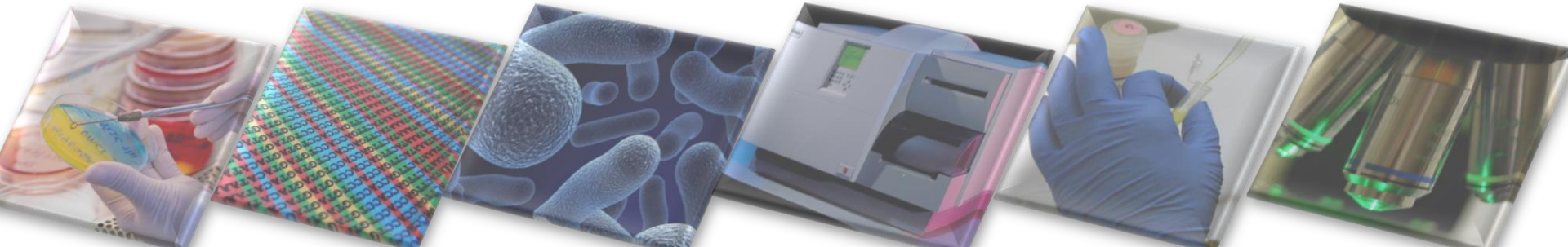
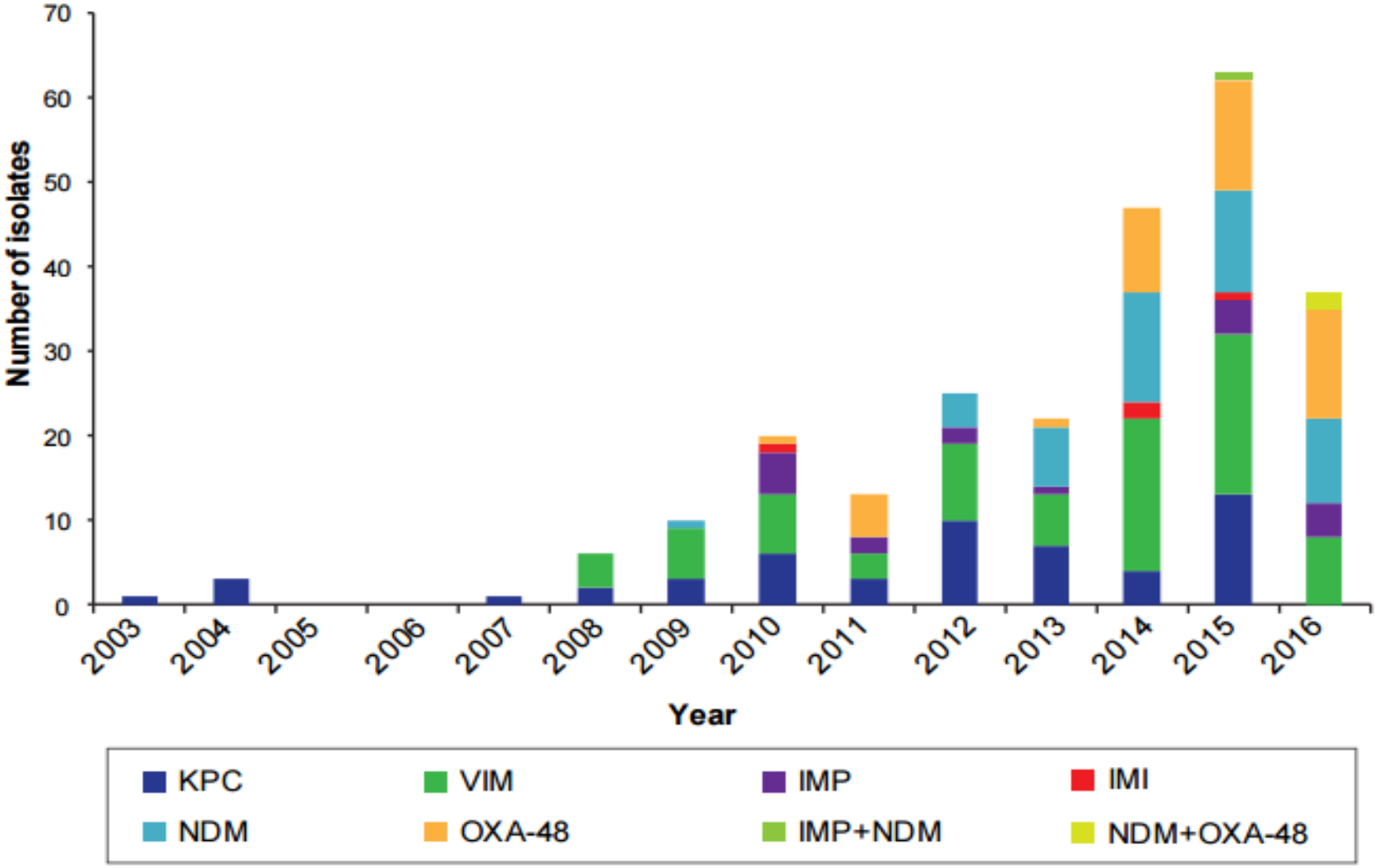
Scottish Microbiology and Virology Network

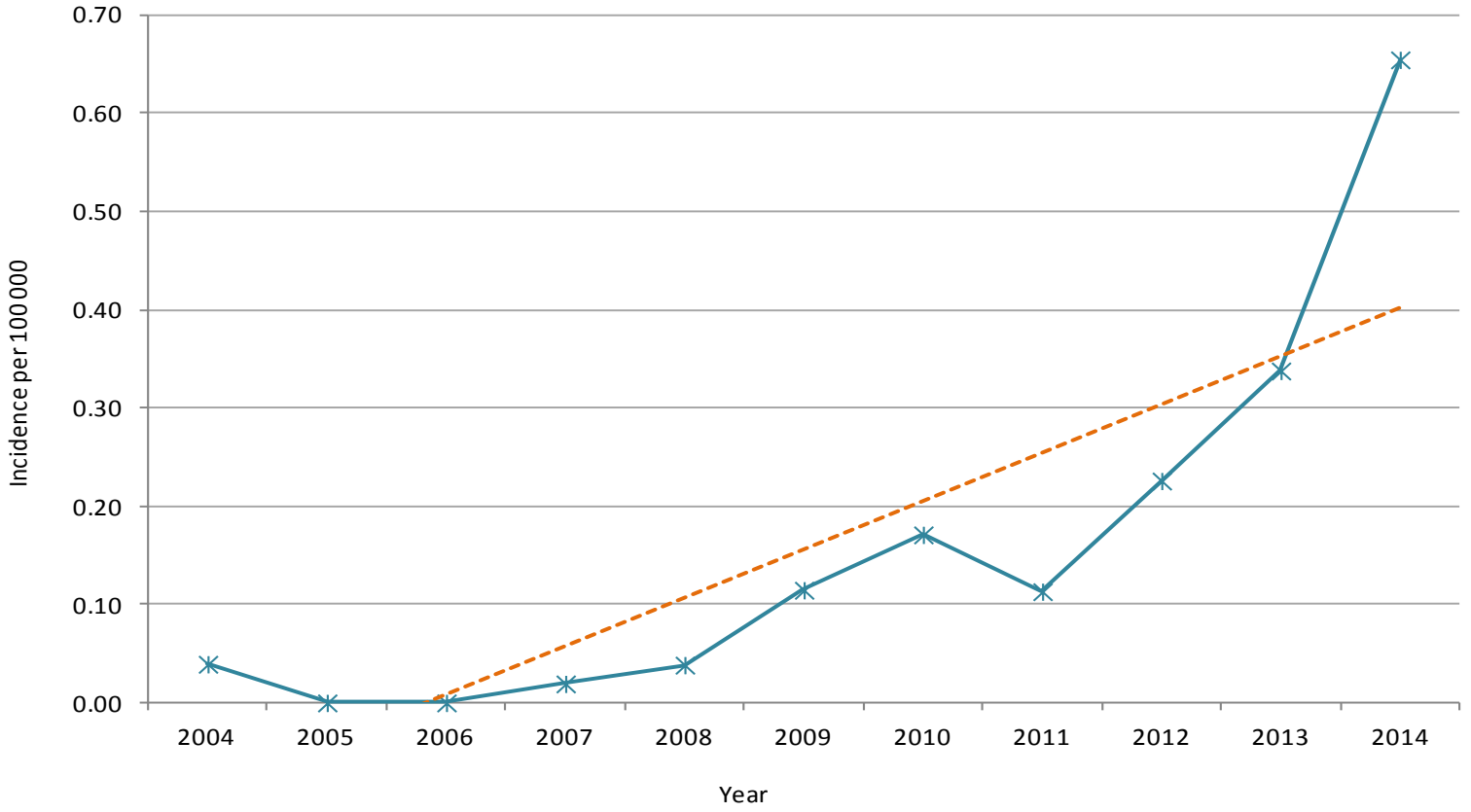
Carbapenemase producers: screening and the new Scottish AMR Satellite Reference Laboratory Service



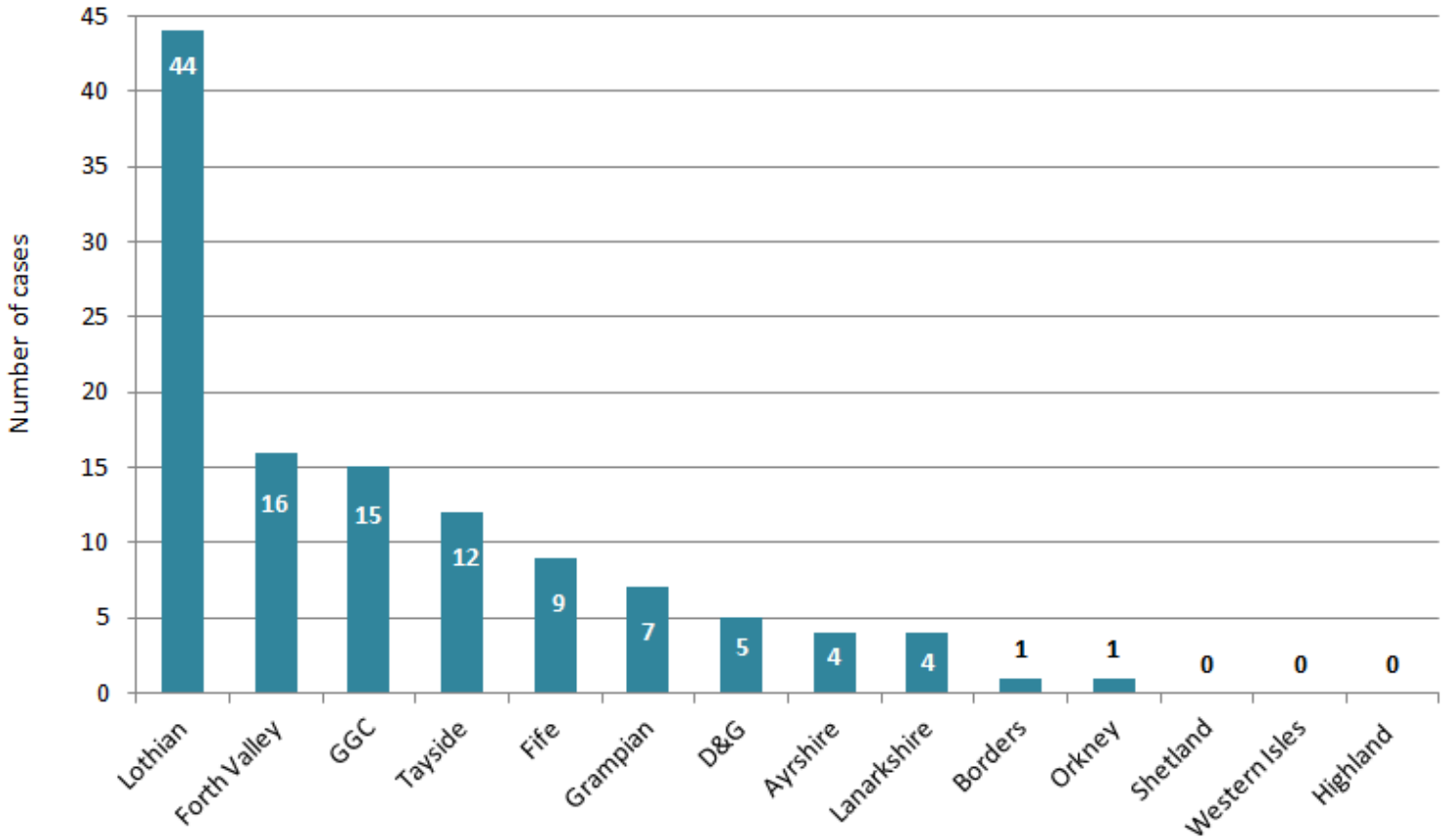
Total number of carbapenemase producing organisms isolated in Scotland from 2003-2016. (2016 data until end of June).



Incidence of CPE cases in Scotland per 100 000 population, 2003-2014



Total CPE cases by board, 2003-September 2015



Age and sex of CPE cases in Scotland 2003- 2015

Age Group	Male		Female		Total	
	N	%	N	%	N	%
<1 month	0	0.0	0	0.0	0	0
1 month - 16 years	1	1.9	3	4.7	4	3.4
17- 64 years	25	46.3	30	46.9	55	46.6
65- 84 years	21	38.9	21	32.8	42	35.6
85 years +	5	9.3	5	7.8	10	8.5
Unknown	2	3.7	5	7.8	7	5.9
Total	**54**	100	**64**	100	118	100

Source or cause of infection/colonisation in cases

Hospital:	
Imported	5
Contact-based transmission	12
Unknown	2
History of carbapenem prescription	1
Total	**20**
Community:	
Imported	1
Unknown	4
Total	**5**

Screening in Numbers

- Compliance with Scottish screening recommendations would result in **24,000** patients being screened each year
- France: Screening **358** NH residents. No CPE found
- Holland: community surveillance: **4,721** assessed, 1,992 stool PCR performed. No CPE found
- Leeds: 6,283 CPE screens on hospital admission. CPE 71 **(1.1%).** x6 increase in screening post-toolkit implementation
- London: Number needed to screen to detect one case:

PCR	CA	NSA
352	589	1,792

so in Scotland 1,000,000 inpatients/yr: = **1,700** cases.

- AMR Ref lab estimate was **500** isolates for confirmation/yr

MacKenzie FM. Rapid screening for carbapenemase producing organisms (CPO) Commercial diagnostic methods: an options paper. Scotland: Scottish Microbiology and Virology Network, 2015
Hayatgheib N. ECCMID OS120 2017; Van de Bunt ECCMID P0413 2017; Horner ECCMID P0422 2017; Batra P0309 ECCMID 2017

CPO diagnostic methods
SMVN recommendations

HISTORY:

- ✓ 2010 – 2015: Various CMO letters recommending CPO screening
- ✓ 2015: SMVN AST Group: Options Paper on CPO detection
- ✓ 2016: HPS Toolkit for CPE screening in acute care.
- ✓ 2016: HIS Evidence Note / Advice Statement
  (insufficient published evidence to recommend a method).

  SMVN AST Group recommends SMI B 60
- ✓ 2017: SMVN produces guidelines based on SMI


23 May 2017

Standardisation of testing for Carbapenemase Producing Organisms (CPO) in Scotland

Version 0.3
23 May 2017

Public Health England

NHS

UK Standards for Microbiology Investigations

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

Scottish Microbiology and Virology Network (SMVN)

Page 1 of 12

SMI = 41 pages long

SMVN guideline:

- Summaries salient points of SMI in 5 pages.
- Information in boxes is mandatory
- Includes Scotland specific information on Reference Laboratory Referrals.

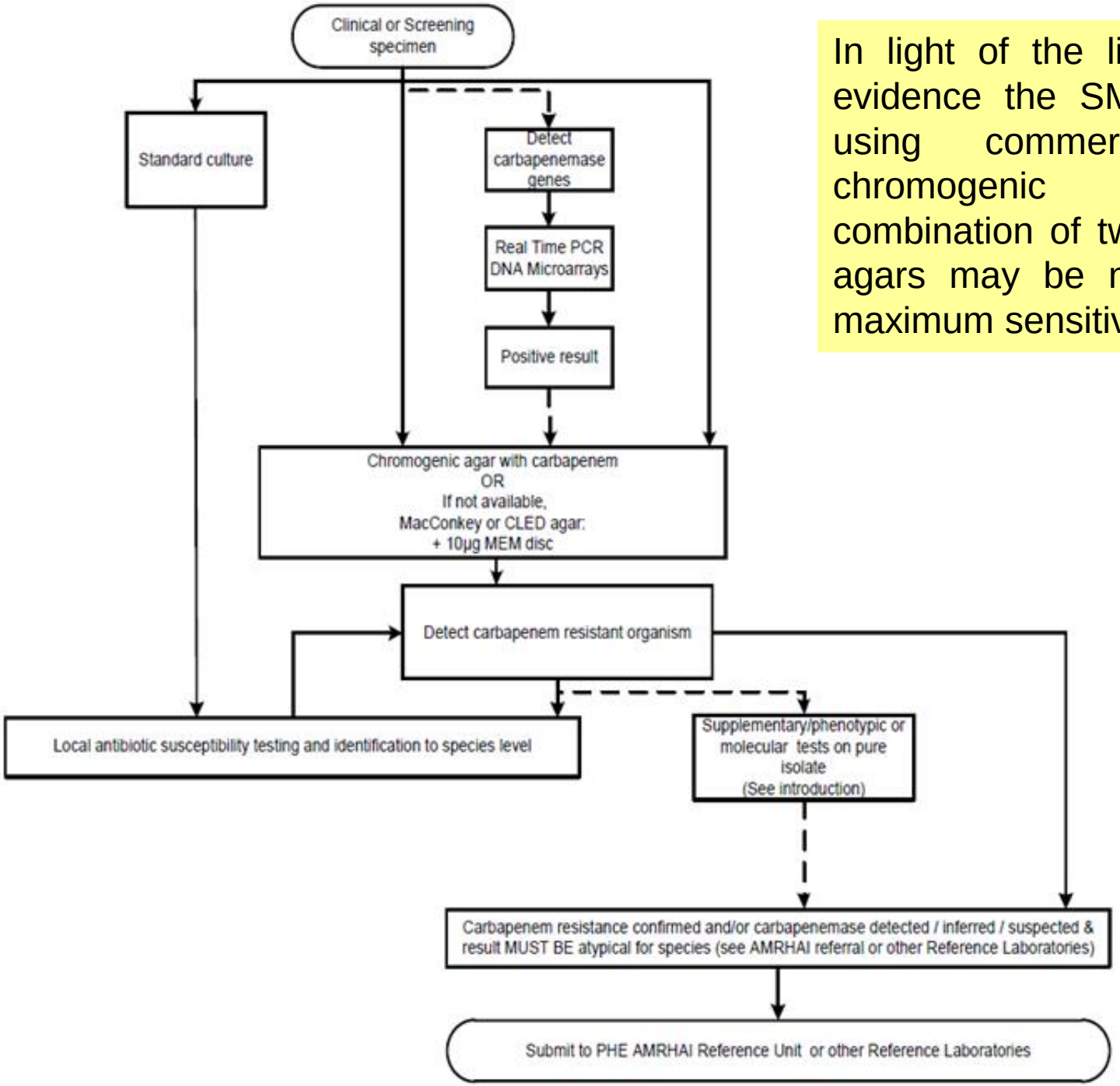
SMVN / SMI recommendations

- All clinically significant isolates of Enterobacteriaceae to tested against a carbapenem. Minimum testing should include:

  a) Isolates from ‘high-risk’ patients according to HPS toolkit

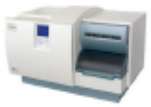
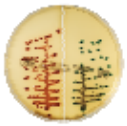
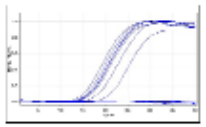
  b) Any isolates found grossly resistant to co-amoxiclav (>32 mg/L) if not screened with a carbapenem.

- EUCAST screening cut-off values to be used.



In light of the limited available evidence the SMI recommends using commercial selective chromogenic agar. A combination of two chromogenic agars may be needed to offer maximum sensitivity.

Results

	Vitek 2		Etest		Disc testing	CARBA NP	CARBA SMART	SuperCARBA	Multiplex PCR
									
	Screening	Clinical	Screening	Clinical					
Sensitivity (95% CI)	99% (95-100)	86% (77-92)	98% (93-100)	70% (60-79)	84% (75-90)	95% (89-98)	91% (83-96)	98% (93-100)	100% (96-100)
Specificity (95% CI)	69% (48-86)	88% (70-98)	58% (37-77)	88% (70-98)	85% (65-96)	62% (41-80)	85% (65-96)	62% (41-80)	100% (88-100)
False negatives	1 OXA-48 - - - -	13 OXA-48 1 VIM - - -	2 OXA-48 - - - -	14 OXA-48 8 VIM 5 KPC 2 NDM 1 IMP	3 OXA-48 8 VIM 2 KPC 1 NDM 2 IMP	3 OXA-48 2 VIM - - -	3 OXA-48 4 VIM 2 KPC - -	- 1 VIM 1 KPC - -	- - - - -
Technical difficulty	++		+		+	+	+	+	+++
Cost	£££		££		£	£££	£	£	££

Carbapenemase producing *Enterobacteriaceae* – the trouble with screening

Emily Goldstein[1], Rory Gunson[1], Katie Hopkins[2], Neil Woodford[2], John Coia[3], Brian Jones[3]

Reporting

The SMVN requires all laboratories to standardise reporting based on the SMI and as follows:

SCREENING SAMPLES FOR CULTURE

Negatives
"Carbapenem-resistant organism **NOT** isolated"

Positives
"Carbapenem-resistant organism isolated. It may produce a carbapenemase; further investigations are being undertaken"

"Carbapenem resistant organism isolated. Carbapenemase production confirmed"

Common reporting codes required – information to follow ASAP.

Reference Laboratory referrals

A. All organisms suspected or newly confirmed to produce a carbapenemase must be referred to the Satellite AMR Reference Laboratory, Glasgow (operational from 3 July 2017)

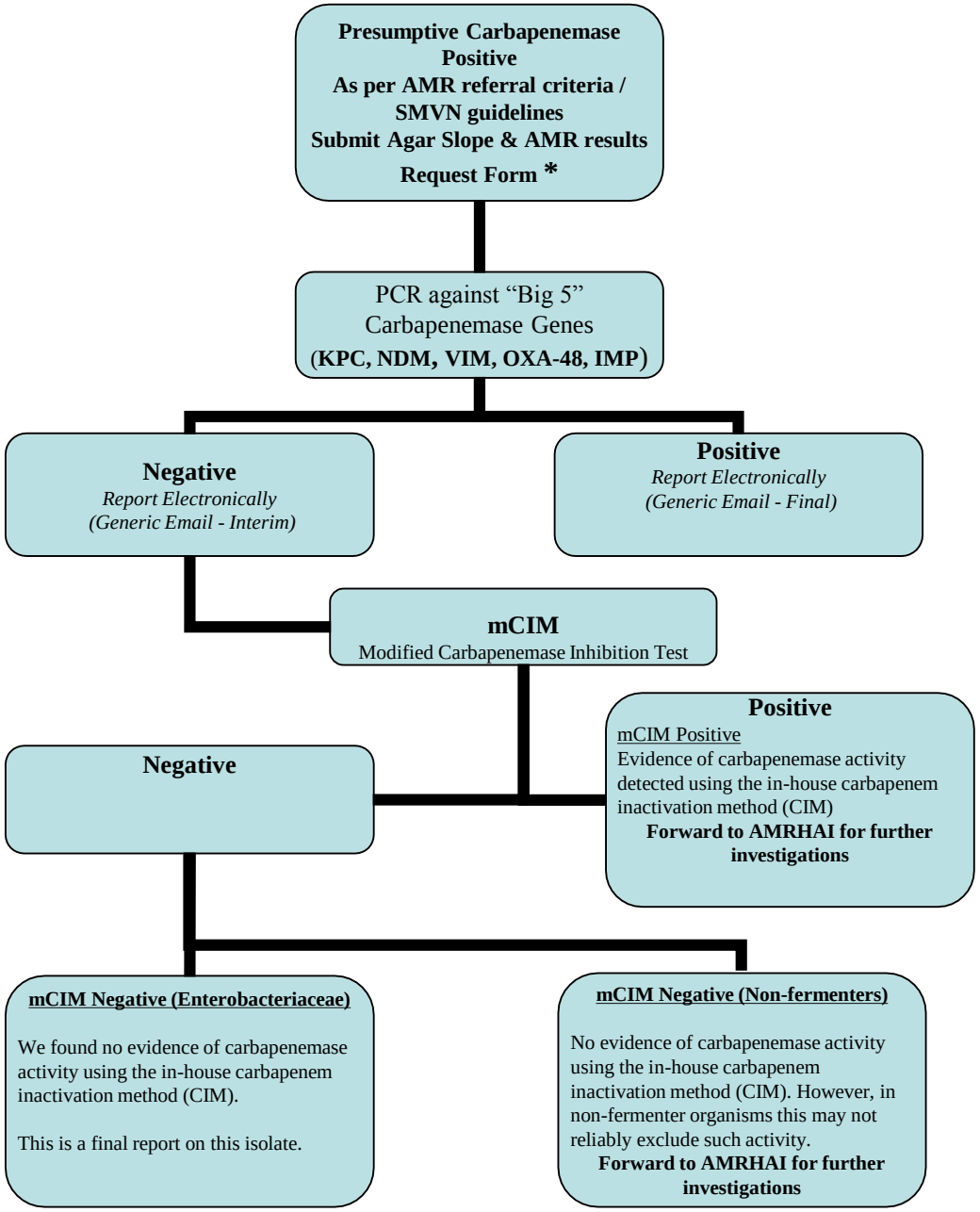
B. Referring laboratories MUST comply with the criteria and requirements stipulated in the referral form to ensure appropriate processing of referred isolates.

Referrals

- Do NOT send isolates of *Enterobacter* that have borderline resistance to ertapenem, but remain fully susceptible to other carbapenems.
- Do NOT send isolates of *Serratia, Morganella* or *Proteus* spp. that are borderline resistant to imipenem, but susceptible to other carbapenems.
- Do send all *Pseudomonas* spp. suspected to produce a carbapenemase, i.e. isolates resistant to carbapenems, ceftazidime, and piperacillin-tazobactam. Do NOT send isolates of *Pseudomonas* spp. resistant only to carbapenems with good susceptibility to other β-lactams.
- Do NOT send isolates of *Pseudomonas* spp. that are resistant to ertapenem, but susceptible to other carbapenems. Ertapenem resistance is inherent in the genus.
- Do send *Acinetobacter* spp. suspected to produce a metallo-carbapenemase, i.e. with an MIC above the EUCAST clinical breakpoint (MIC >8mg/l for meropenem)
- Do NOT send isolates of *Acinetobacter* that are resistant to ertapenem, but susceptible to other carbapenems. Ertapenem resistance is inherent in the genus.
- Do NOT send isolates of *Stenotrophomonas maltophilia, Aeromonas* spp. , *Myroides* spp., *Elizabethkingia meningoseptica* and '*chryseobacteria*' for investigation of carbapenem resistance because metallo-carbapenemase production is an intrinsic characteristic of these bacteria.

Analytical service

- Confirmation of ID & sensitivities
  - Purity plate, ID (MALDI-TOF)
- Confirmation of “Big 5” Carbapenemases
  - Real-time Multiplex (Validated AMRHAI assay) for: **KPC, OXA-48, NDM & VIM**
  - Real-time for **IMP** using AMRHAI primers
  - Already used within GGC
- Archiving of isolates at -80C
- Electronic reporting of result on day of receipt


Presumptive Carbapenemase Positive
As per AMR referral criteria / SMVN guidelines
Submit Agar Slope & AMR results Request Form *
PCR against "Big 5" Carbapenemase Genes
(KPC, NDM, VIM, OXA-48, IMP)
Negative
Report Electronically
(Generic Email - Interim)
Positive
Report Electronically
(Generic Email - Final)
mCIM
Modified Carbapenemase Inhibition Test
Positive
mCIM Positive
Evidence of carbapenemase activity detected using the in-house carbapenem inactivation method (CIM)
Forward to AMRHAI for further investigations
Negative
mCIM Negative (Enterobacteriaceae)
We found no evidence of carbapenemase activity using the in-house carbapenem inactivation method (CIM).
This is a final report on this isolate.
mCIM Negative (Non-fermenters)
No evidence of carbapenemase activity using the in-house carbapenem inactivation method (CIM). However, in non-fermenter organisms this may not reliably exclude such activity.
Forward to AMRHAI for further investigations

Conclusions

- Cases of CPE in Scotland have significantly increased since reporting began in 2003.

- Limitations:
  - compliance with screening,
  - referral to AMRHAI,
  - not representative of admission population

- There is currently a limited picture of the epidemiology of CPE in Scotland.

- New AMR Satellite laboratory will allow for more accurate picture of CPE epidemiology