BRITISH SOCIETY FOR ANTIMICROBIAL CHEMOTHERAPY

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Diagnostic stewardship

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Introduction – the clipboard audit

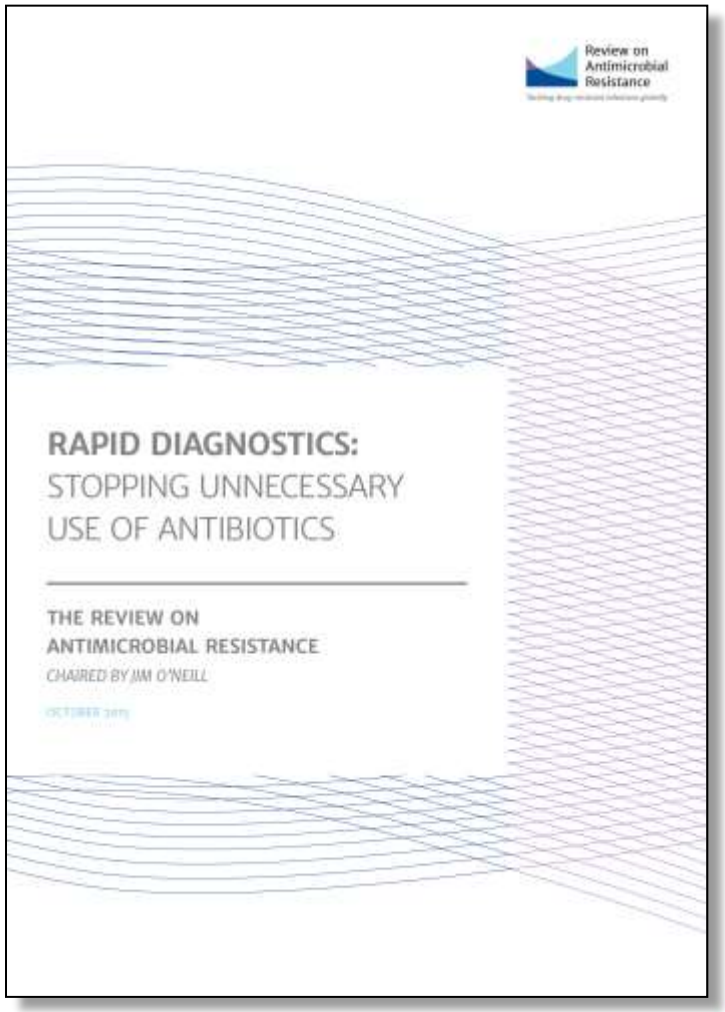
- Audits of antibiotic prescribing often assess compliance with a specific treatment guideline
  (e.g. UTI or community acquired pneumonia)
- An assumption is made that the original diagnosis was correct
- If you have got the diagnosis wrong, how can you prescribe the right treatment?

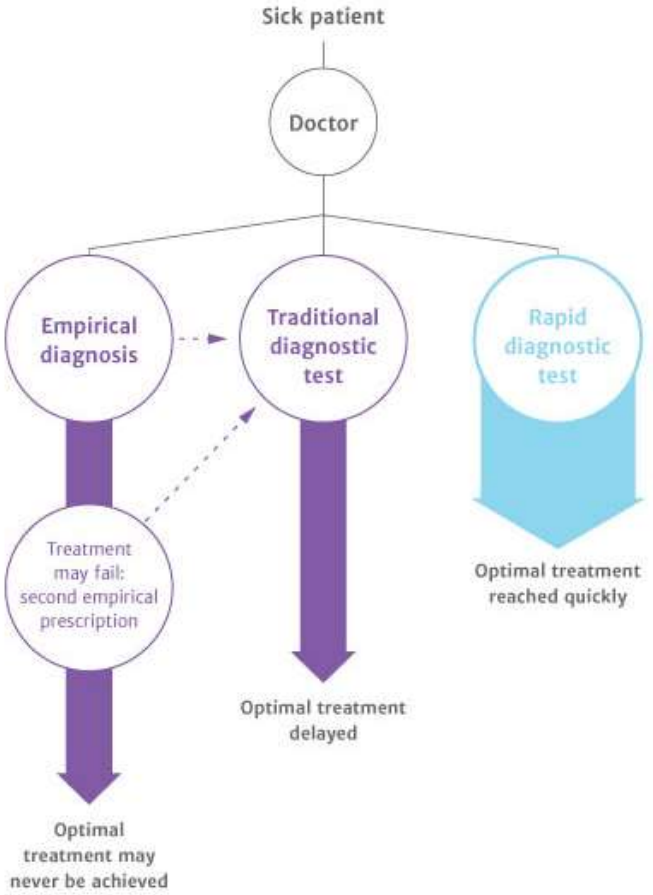
Limitations of current antibiotic prescribing

- Remains empirical (i.e. ‘best guess’)
- Diagnostic uncertainty compounded by antibiotic resistance
- Potential consequences:
  - Wrong organism targeted
  - Wrong antimicrobial agent selected
  - Unnecessary exposure to side effects
  - Expenditure without benefit

Adapted from Finch, EU Interdepartmental conference 2005

AMR Review by J O'Neill

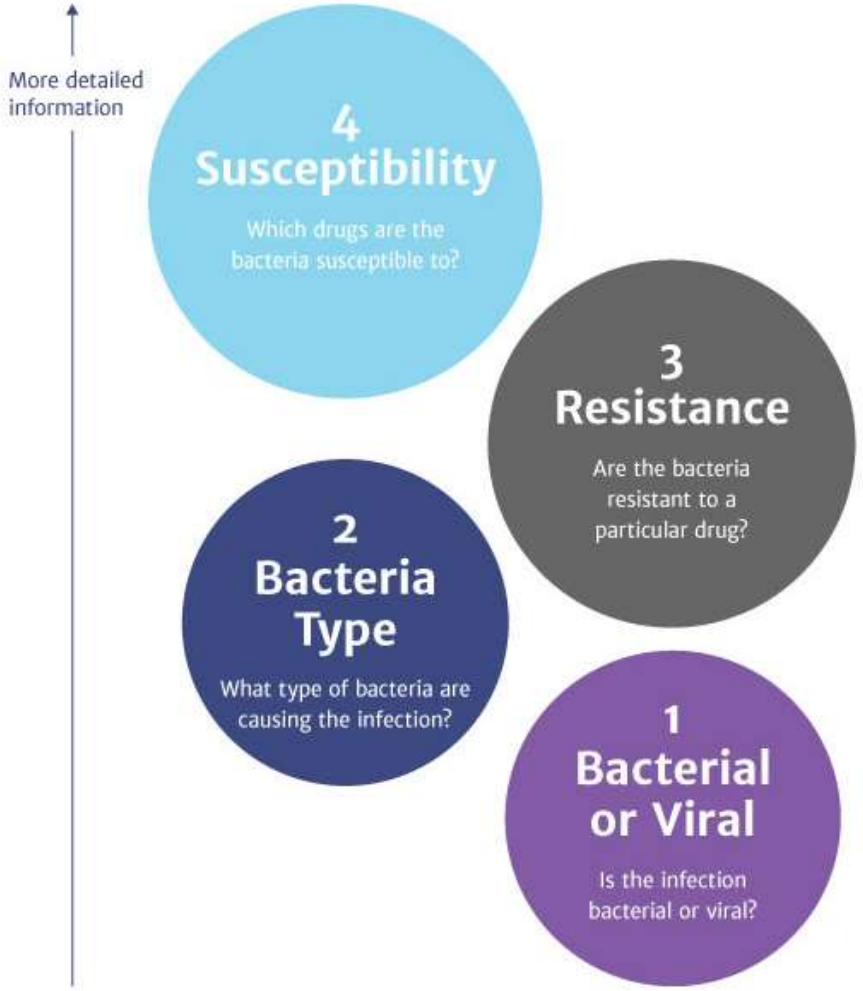




Review on Antimicrobial Resistance

https://amr-review.org

What rapid diagnostics could test

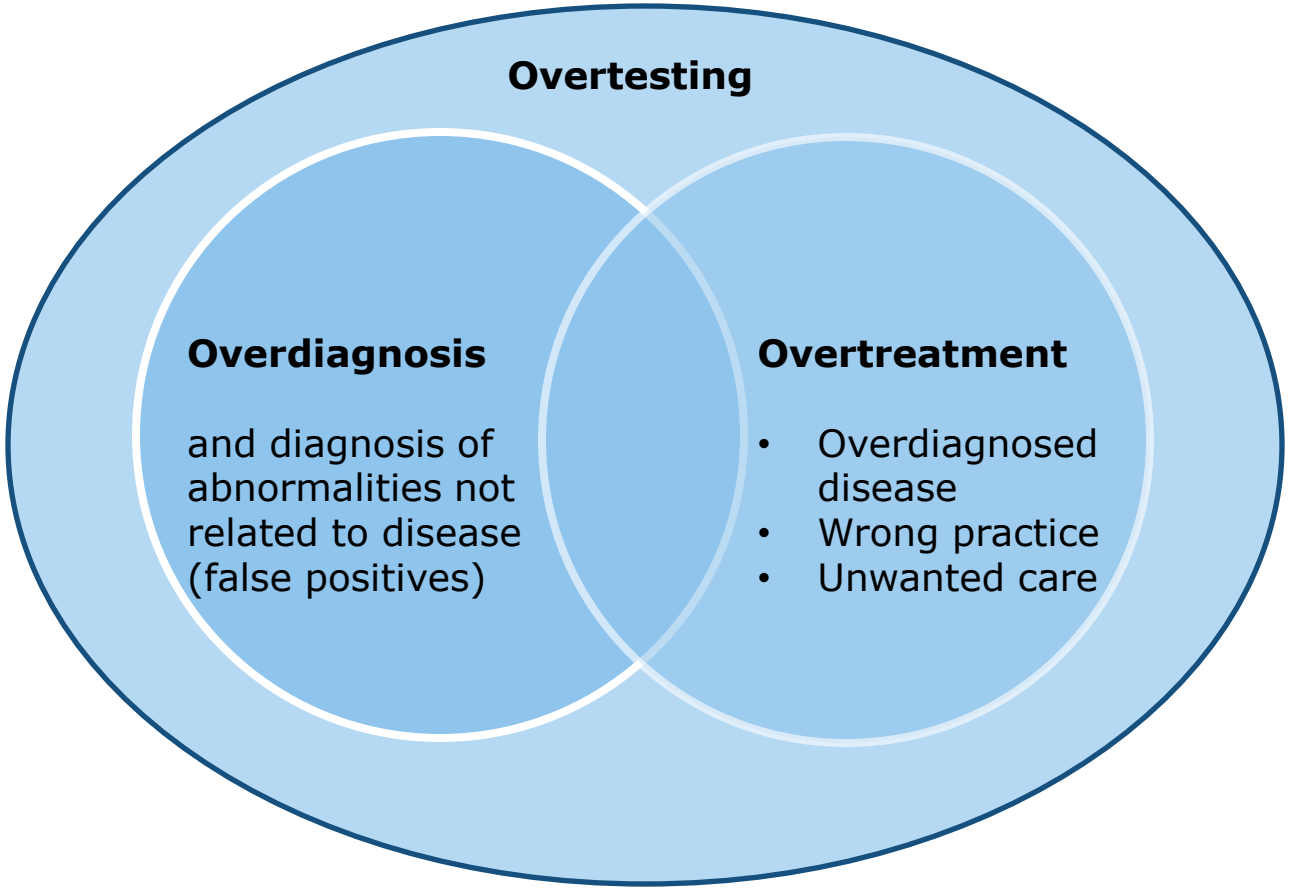


https://amr-review.org

Review on Antimicrobial Resistance

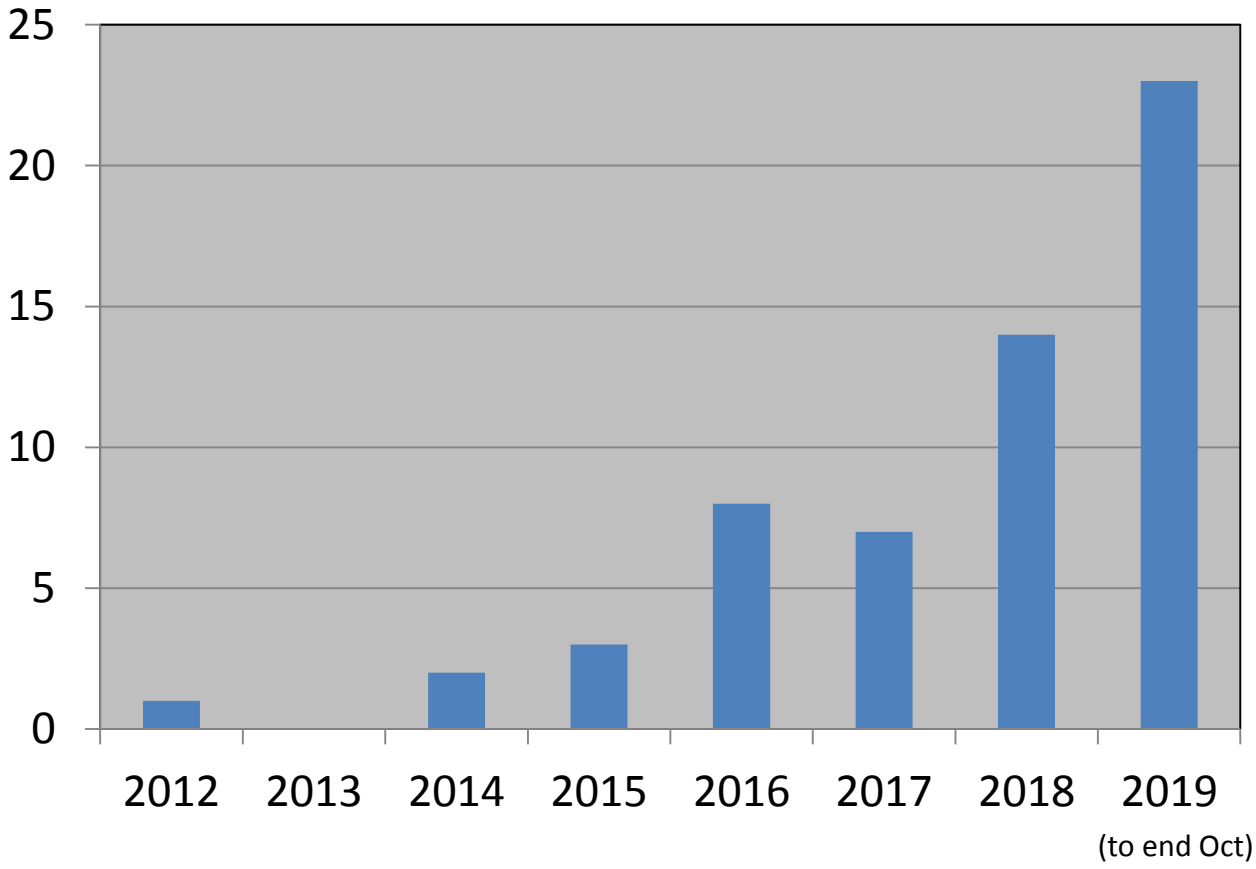
Most use of antibiotics in humans is to treat an infection that they haven't got

Overuse of diagnostic tests



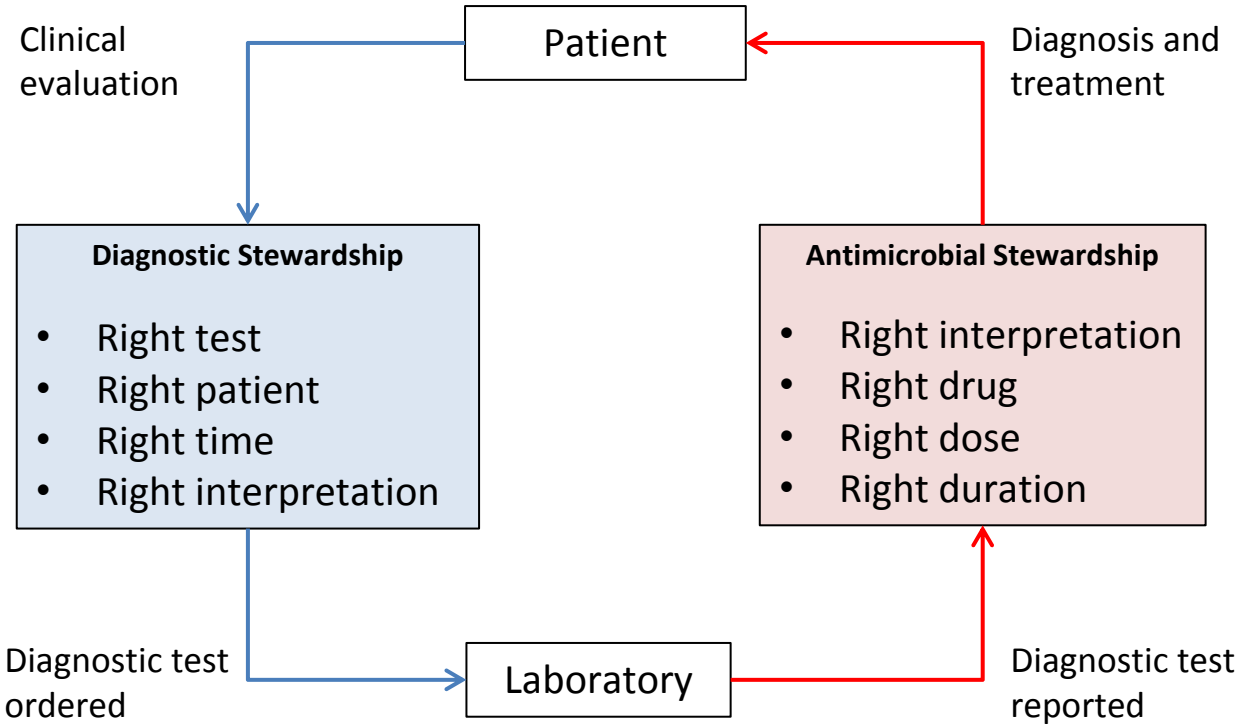
Adapted from: Morgan DJ et al. BMJ 2015; 351: h4534

PubMed citations with the term ‘Diagnostic Stewardship’ in the title field



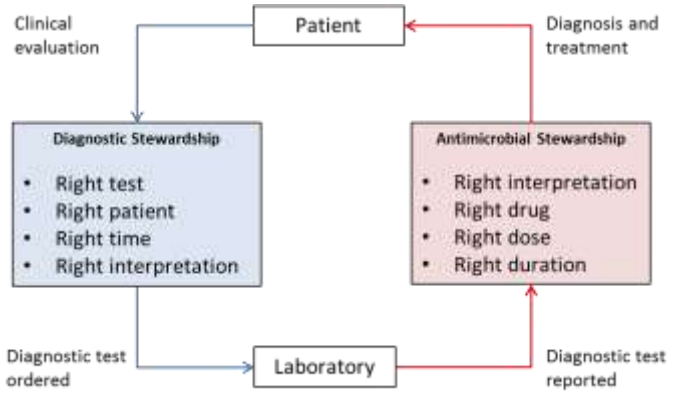
Approach to diagnostic testing

Diagnostic stewardship view



Messacar K et al. *J Clin Microbiol* 55:715–723.

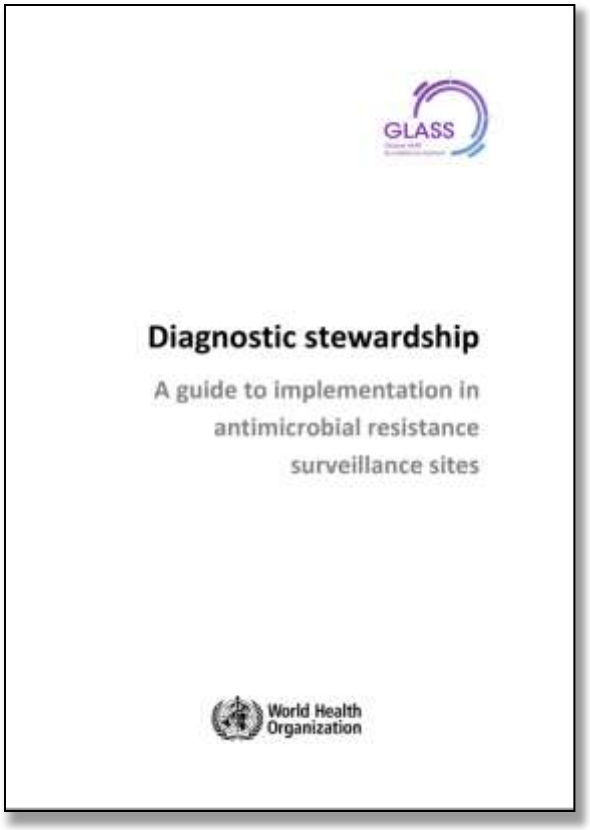
Approach to diagnostic testing



Right test	Is the test appropriate for the clinical setting?
Right patient	Will the clinical care of the patient be affected by the test result?
Right time	Will the result be available in time to affect patient care optimally?

Messacar K et al. *J Clin Microbiol* 55:715–723.

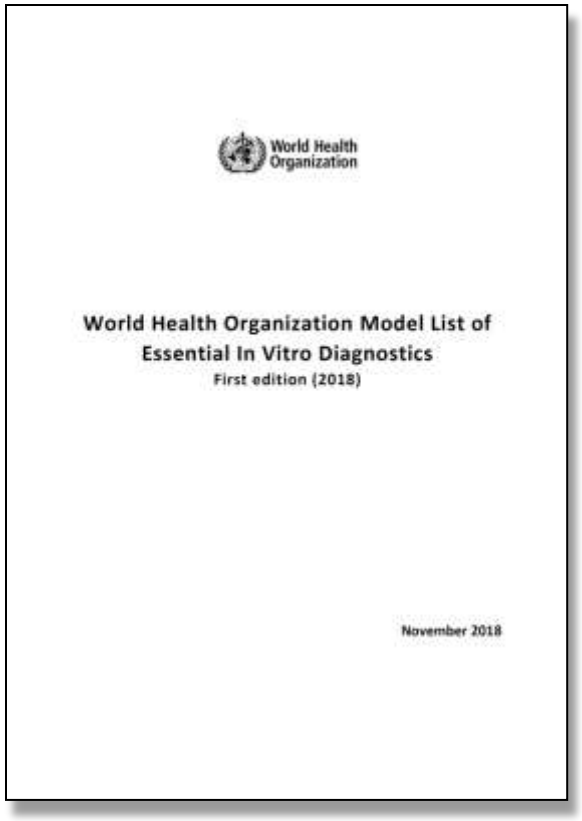
WHO Guide to Diagnostic Stewardship



Guide to support robust microbiological diagnosis, including antimicrobial susceptibility testing (AST) in countries participating in surveillance

https://www.who.int

WHO Essential Diagnostics List



Objectives

- In vitro diagnostics (IVDs) that are recommended for use in a tiered national health care system
- Not intended to be prescriptive
- Countries make own decisions based on national or regional burden of disease, unmet needs and priorities
- Informs UN agencies and NGOs that support selection, procurement, supply, donations or provision of IVDs.
- Informs medical technology private sector on IVD priorities and the IVDs needed to address global health issues.

https://www.who.int

WHO Essential Diagnostics List 2018

Primary health care

General IVDs	Urine dipstick and urine microscopy Microscopy of disease appropriate specimens (e.g. venous whole blood, urine, stool, etc.)
Disease-specific IVDs	Hepatitis B HIV Malaria Tuberculosis Syphilis

Health care facilities with clinical laboratories

General IVDs	Urine dipstick and urine microscopy Culture of disease appropriate specimens (e.g. venous whole blood, urine, stool, etc.) Blood culture Antimicrobial susceptibility testing
Disease-specific IVDs	Hepatitis B HIV Malaria Tuberculosis Syphilis

Approach to diagnostic testing

The traditional laboratory science view

Pre-analytical	Analytical	Post-analytical
Test selection Ordering Collection Transport	Processing Testing Test performance	Interpretation Reporting Intervention

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Diagnosing UTI

NICE
Urinary tract infection (lower) – women (Oct 2019)

- **If the woman is under 65y of age and does not have risk factors for complicated UTI, a urine dipstick can be used as an aid to diagnosis** – dipstick is unreliable in women aged older than 65y and those who are catheterised

- **A sample should be sent for urine culture in all women with suspected lower UTI who:**
  - Are pregnant
  - Are older than 65y
  - Have symptoms that are persistent or do not resolve with antibiotic treatment
  - Have recurrent UTI (2 episodes in 6 months or 3 in 12 months)

To Dip Or Not To Dip?

- Project lead by Elizabeth Beech (Pharmacist)
- Project undertaken in 2015-16 to improve UTI management in Care Homes
- An audit in 2013 had shown that 115 of 347 residents had received 208 antibiotic prescriptions for UTI
- More than half were diagnosed on basis of urine dipstick testing
- Large number of prescriptions were for ciprofloxacin and cephalosporins

What did they do about it?

- Introduce an education bundle in care homes emphasising the limitations of using urine dipstick alone in assessing residents (23 care homes providing care for ~800 residents)
- Use NICE / SIGN 88 guideline to develop better, structured documentation for UTI diagnosis
- Monitor for unintended consequences
  e.g. episodes of urosepsis requiring hospitalisation

Guidance for Care Home staff for older patients (>65) with a suspected UTI

- Complete and fax to GP surgery. File original in patient notes.
- **DO NOT PERFORM URINE DIPSTICK** – No longer recommended in pts >65 yrs
- CLEAR URINE – UTI highly unlikely
- Consider MSU where possible if ≥ 2 or more signs of infection - UTI likely

Patient:..... **DOB:**.....

Nursing Home:.....

Date:..... **Carer:**.....

Signs of any other infection source? Circle any new symptoms which apply:

Cough Shortness of breath Sputum production Nausea/vomiting Diarrhoea Abdominal pain Red/warm/swollen area of skin

Patients who can communicate symptoms:

NEW ONSET Sign/Symptom	What does this mean?	Tick if present
Dysuria	Pain on urinating	
Urgency	Need to pass urine urgently/new incontinence	
Frequency	Need to urinate more often than usual	
Suprapubic tenderness	Pain in lower tummy/above pubic area	
Haematuria	Blood in urine	
Polyuria	Passing bigger volumes of urine than usual	
Loin pain	Lower back pain	

Catheter?
Y / N
If **YES:**
Reason for catheter:

Temp / Perm

Date changed:

All Patients:

Sign/Symptom	Tick if present	
Temperature above 38.3 or below 36 or shaking chills (rigors)in last 24 hours		
Heart Rate >90		
Respiratory rate >20		
Blood glucose >7.7		Diabetic? Y / N
Bloods taken?		WCC: CRP:
New onset or worsening confusion or agitation		

Management Decision:

- Review in 24 hours
- Mid Stream Urine specimen
- Antibiotic prescription for UTI: Nitrofurantoin (eGFR>45ml/min) Trimethoprim .....
- Other .....

21/11/2014 NHS Bath and North East Somerset CCG

Results

- **56% reduction** in the proportion of residents who had an antibiotic for a UTI

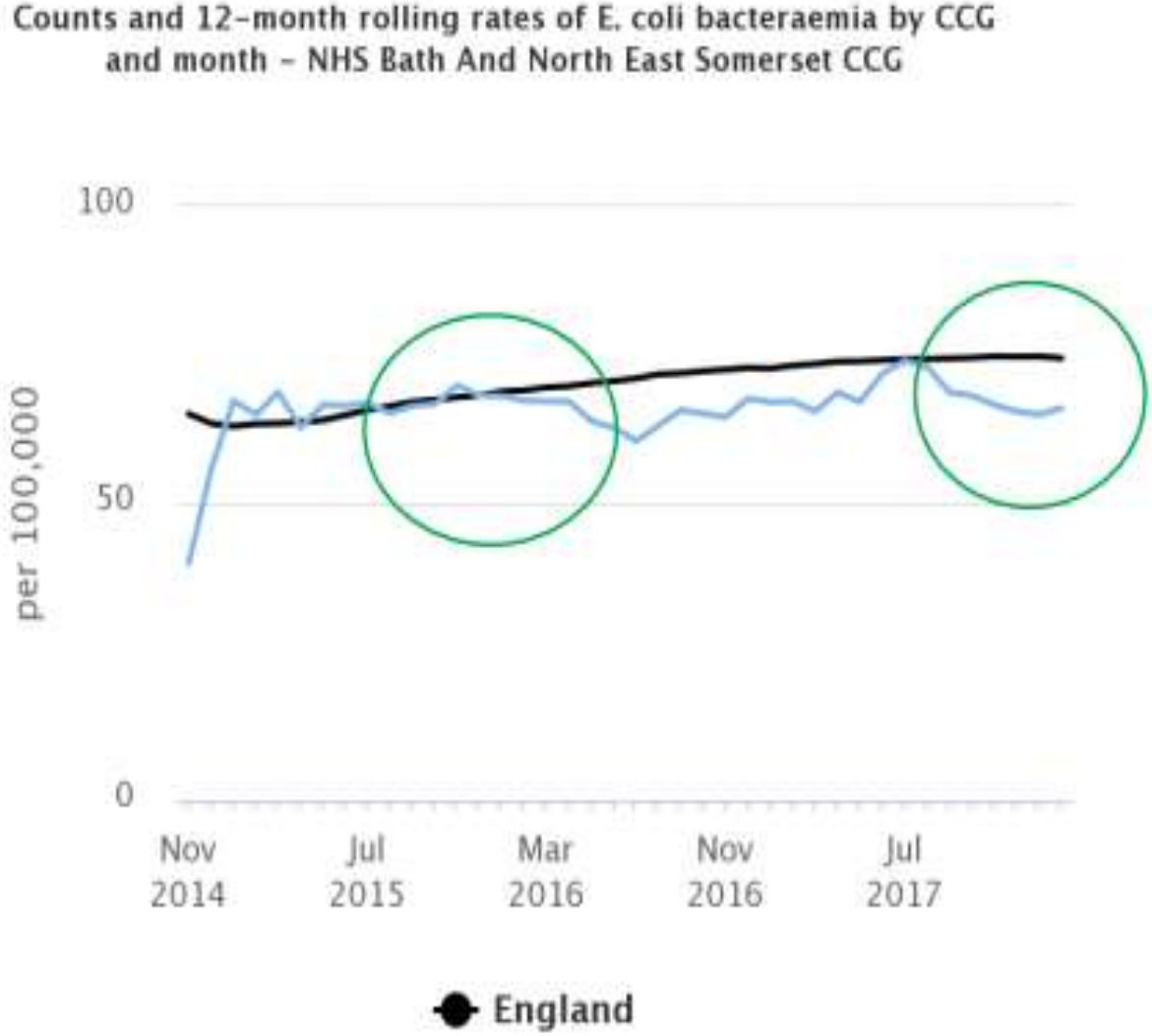
- **67% reduction** in the number of antibiotic prescriptions

- **82% reduction** in the number of residents prescribed antibiotic prophylaxis

- Reduction in unplanned admissions for UTI, urosepsis and acute kidney injury

- Reduced calls to GP practices for inappropriately diagnosed UTI

Educational bundle delivered to all nursing homes



Intervention to reduce treatment of urinary catheter–associated asymptomatic bacteriuria

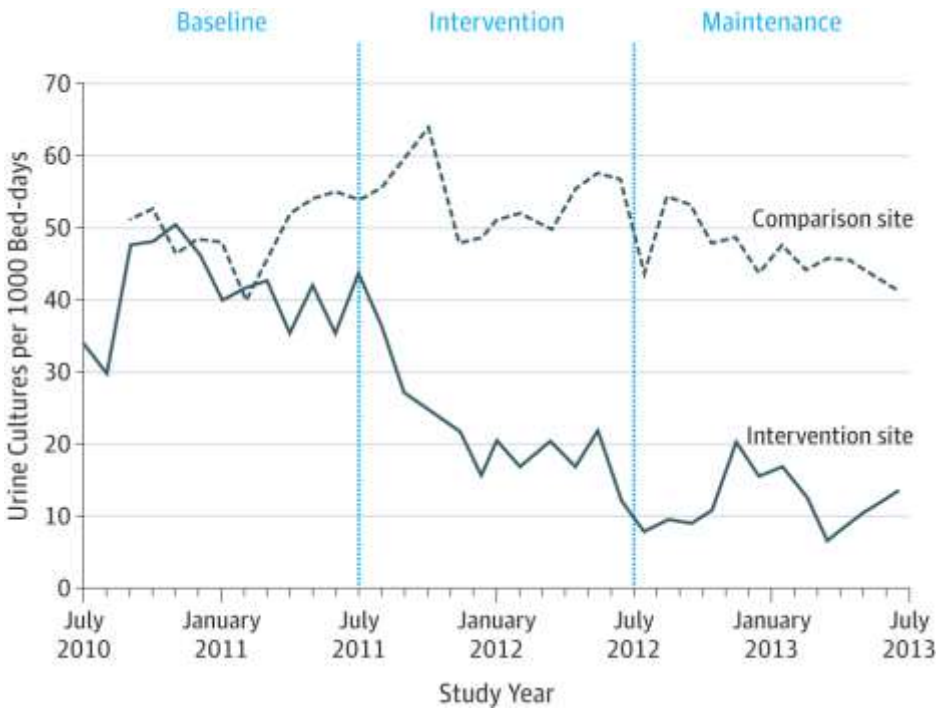
Two outcomes studied:

- Decision to send a sample (unnecessary screening) and the decision to treat a positive result (overtreatment)

Main findings:

- Reduced sampling
- Decrease in treatment of asymptomatic bacteriuria

  1.6 to 0.6/1,000 bed days
- No change in treatment of CAUTI



Trautner BW et al. *JAMA Intern Med*. 2015;175:1120-27

Selective urine culture and antibiotic utilisation

Reflex protocol in 500 ICU patients

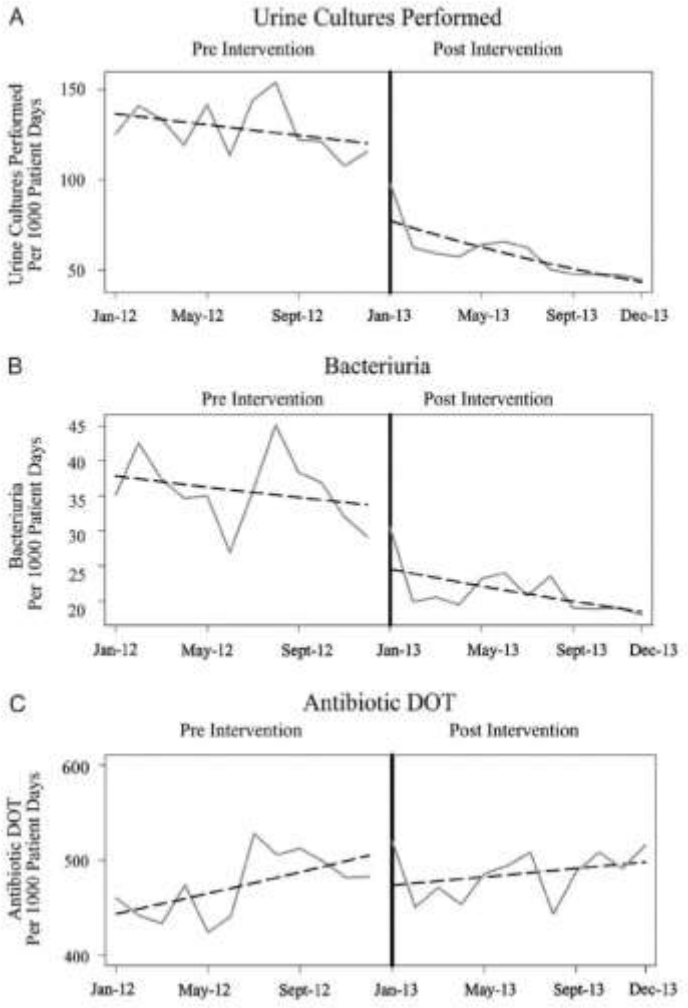
Culture only if >10 wbc/hpf

Results:

- Fewer cultures
- Lower bacteriuria rates
- No change in overall antibiotic days of therapy (DOT)
- Fewer antibiotic starts for index urine culture

Pre: 55/134 (41%) vs.

Post: 28/123 (23%) (p=0.002)



Sarg M et al. *Infect Control Hosp Epidemiol*. 2016; 37: 448–454

Approach to diagnostic testing

The traditional laboratory science view

Pre-analytical	Analytical	Post-analytical
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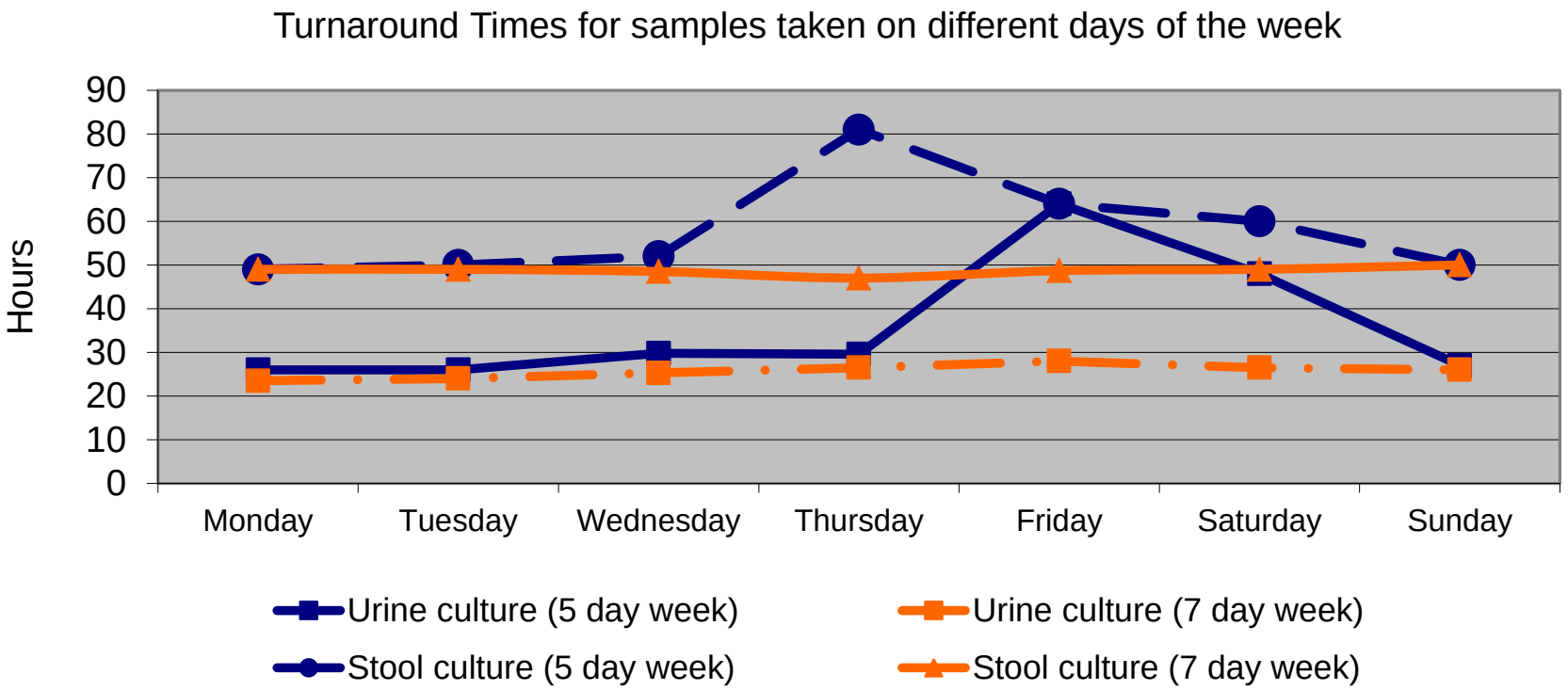
Working patterns: a standard 5 day lab service versus 7 day lab service



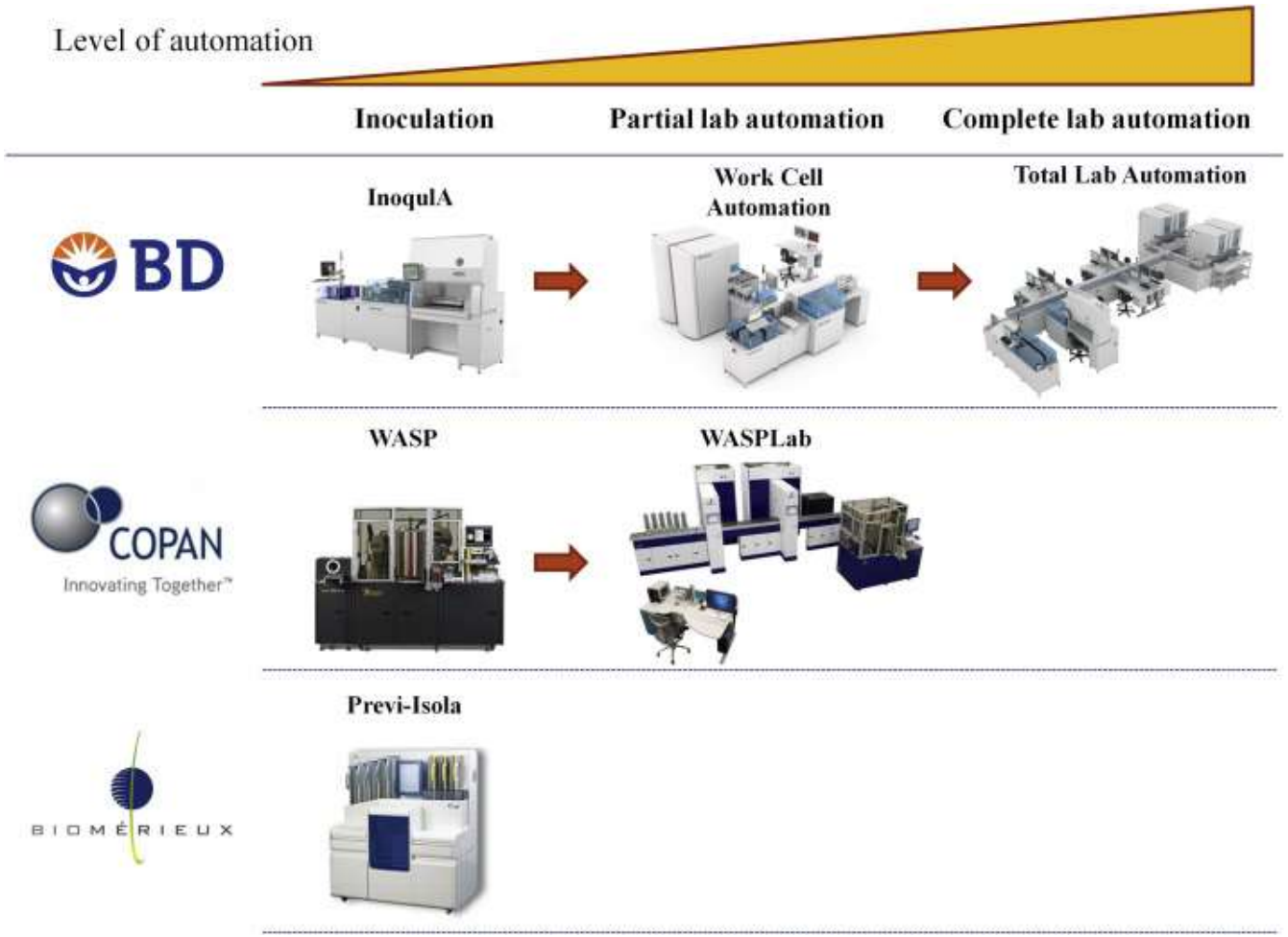
Data from routine laboratory quality indicators, Cambridge

The Bacteriology Laboratory

Cambridge laboratory c. 1987

Fleming's laboratory c. 1929

Levels of automation in bacteriology

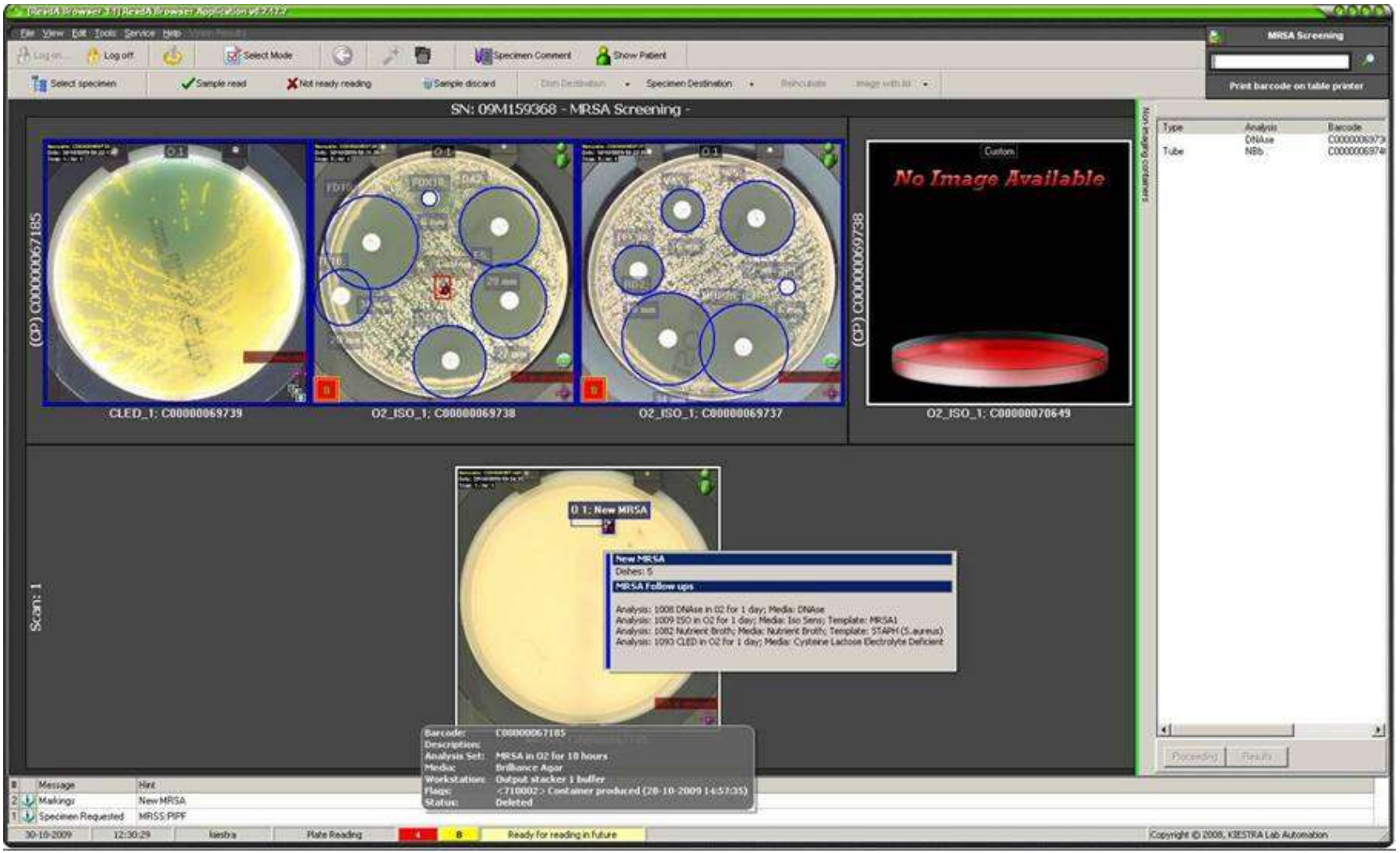


Croxatto A et al. *Clin Microbiol Infect* 2016; 22: 217-235

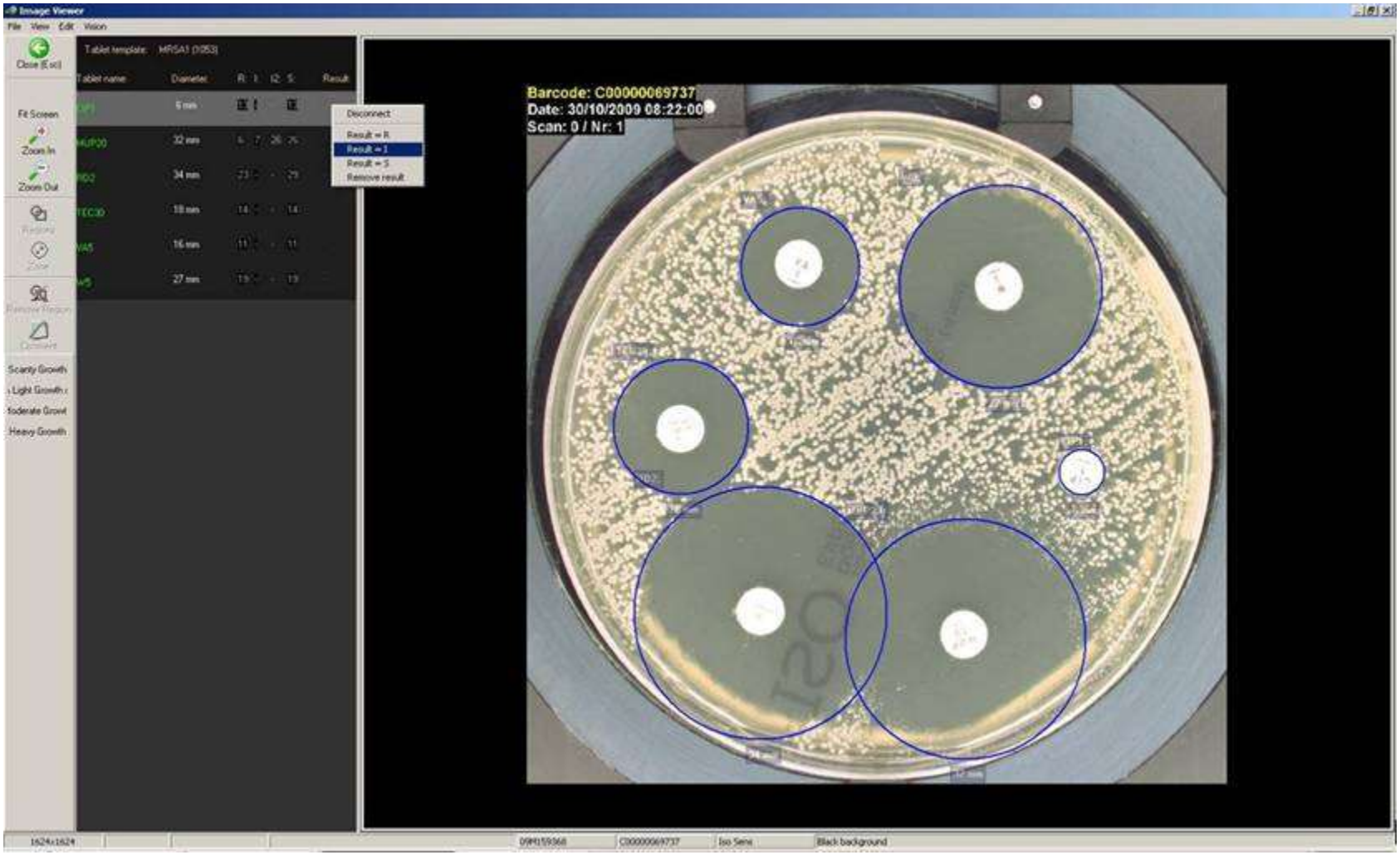
The new Bacteriology Laboratory

Cambridge laboratory 2013

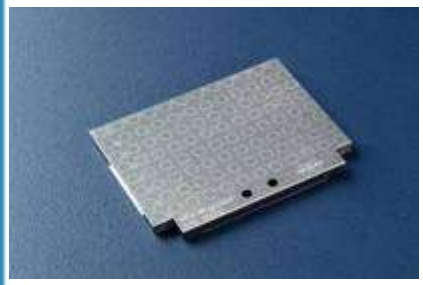
Allows us to store images

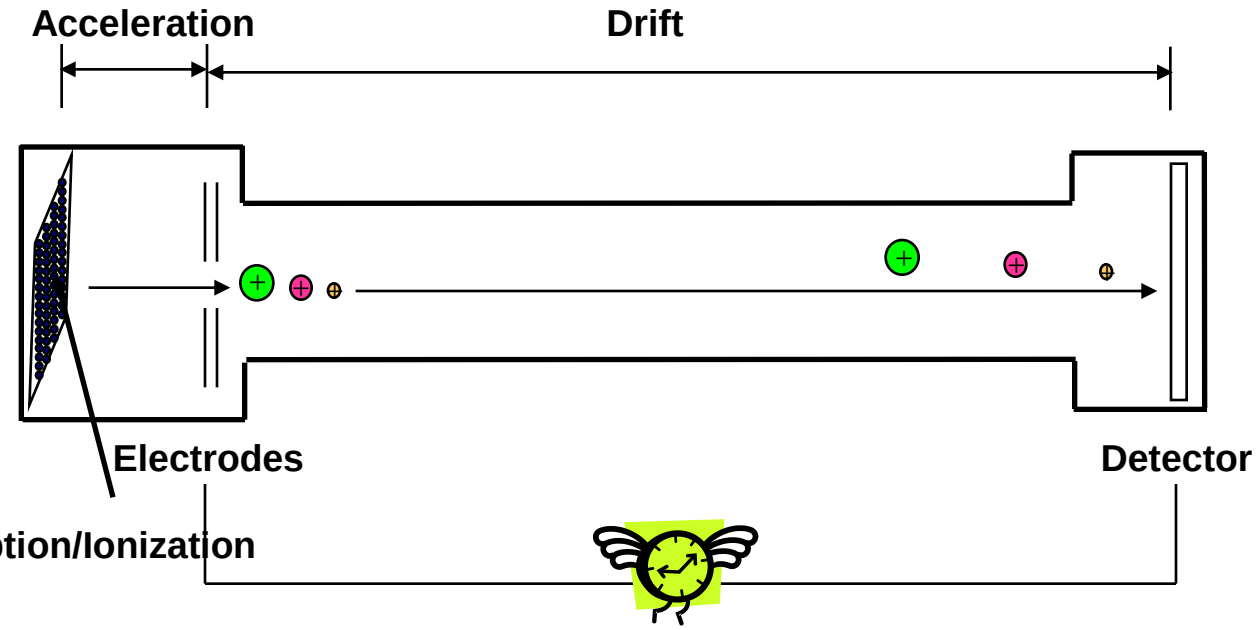


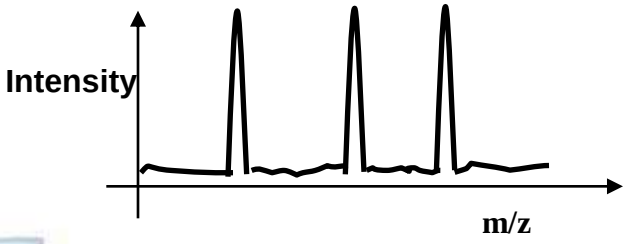
Record susceptibility test images and zone sizes



MALDI-TOF Mass Spectrometry

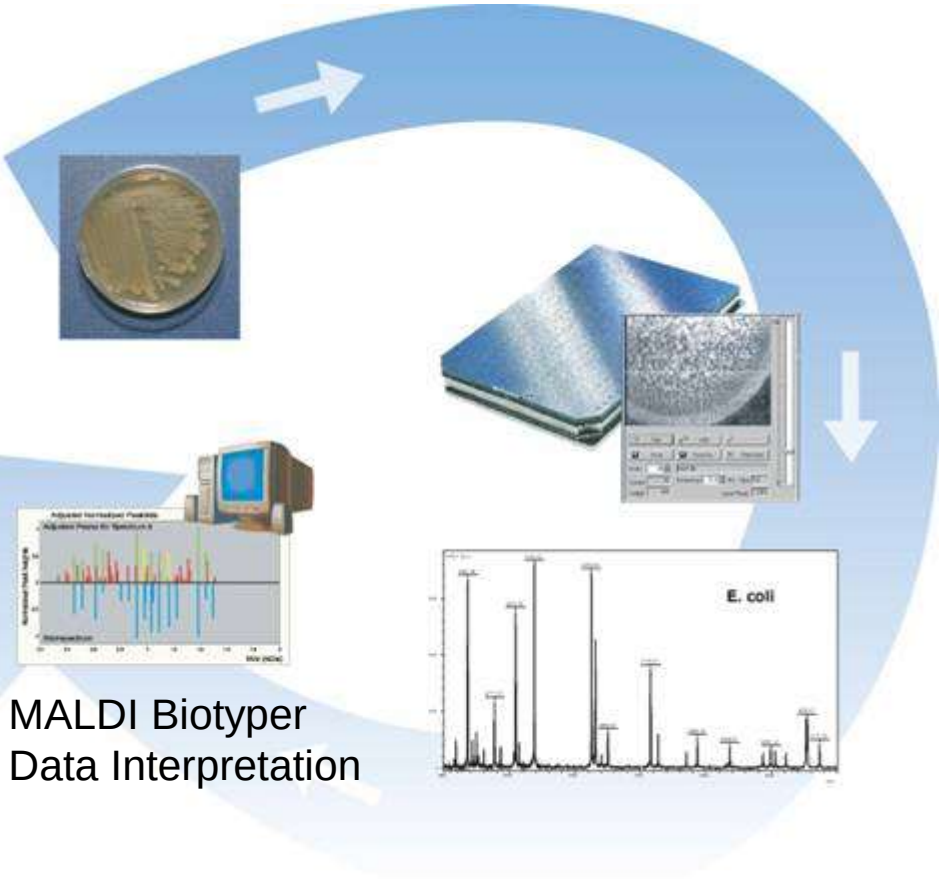






Modified from: Lottspeich, Zorbas, eds
"Bioanalytik", Spektrum Akademischer Verlag, 1998

MALDI Biotyper - Workflow

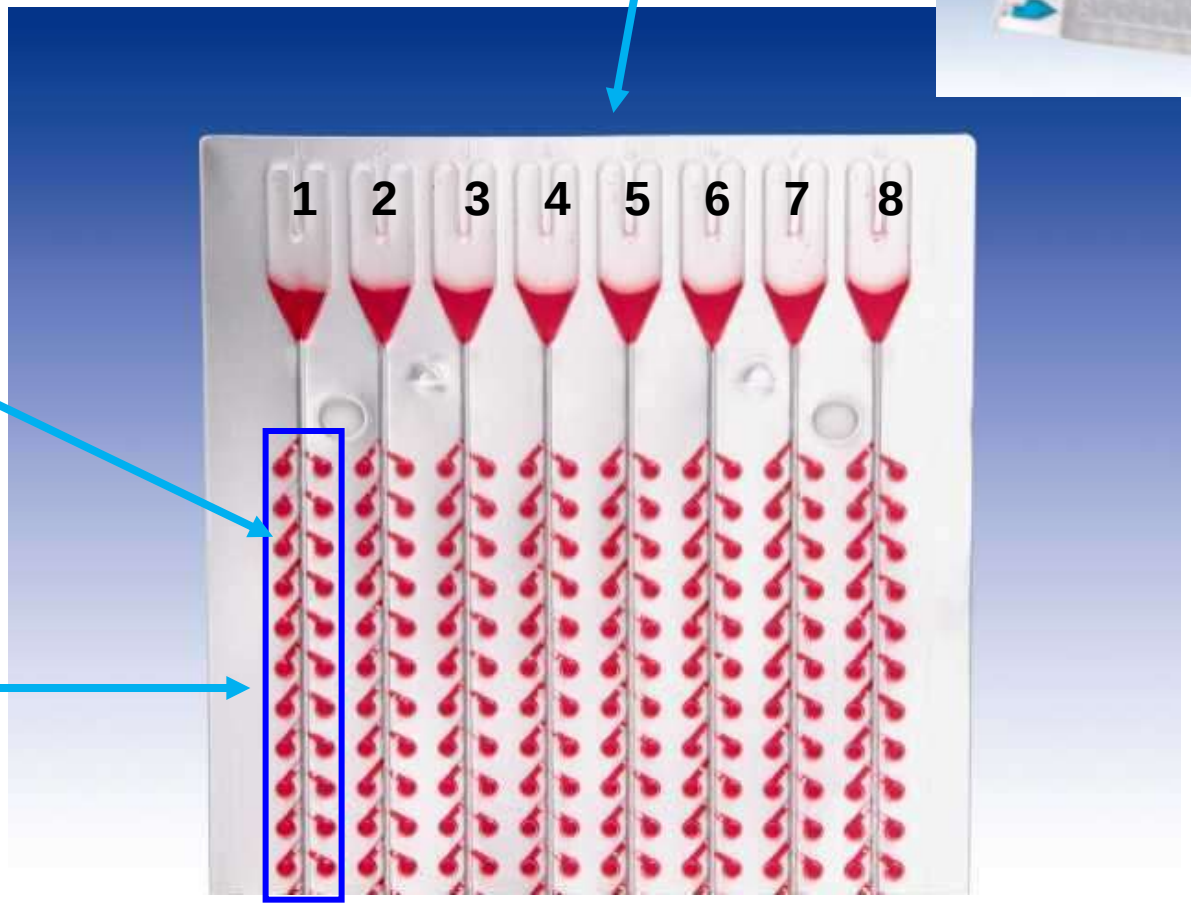


TaqMan® Array Cards

1 to 8 samples

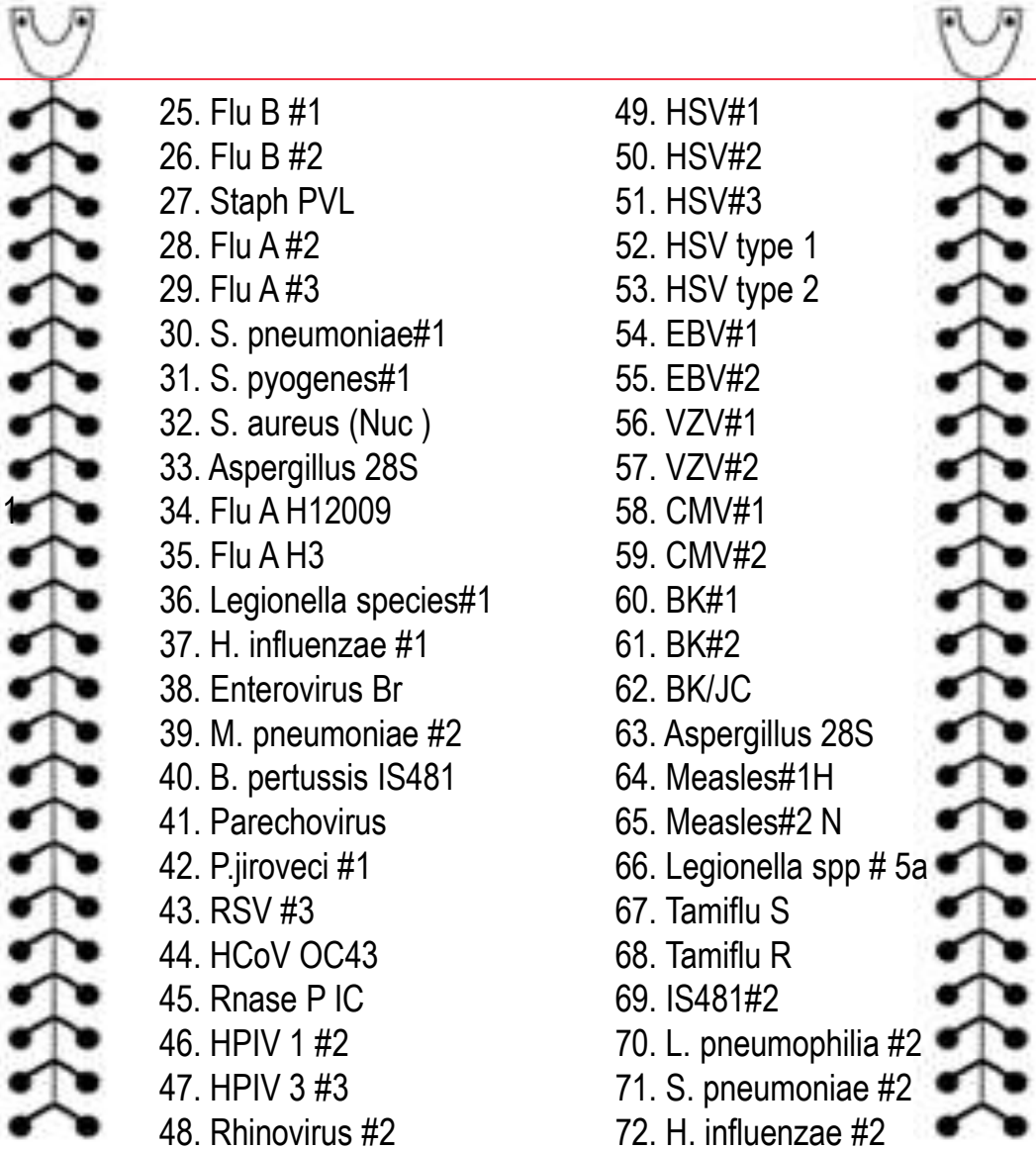
TaqMan® Assays pre-spotted

48 wells per channel



384 wells (1µL reaction volume)

Respiratory Card: Version 9 – ECMO



1. RSV A
2. RSV B
3. HPIV 1
4. HPIV 2
5. HPIV 3
6. HPIV 4
7. Enterovirus
8. Rhinovirus
9. B. pertussis ptx S1
10. HCoV OC43/HKU1
11. 18S RNA
12. HCoV NL63
13. HCoV 229E
14. hMPV
15. MS2 IC
16. Adenovirus #1
17. Bocavirus
18. Adenovirus #2
19. L. pneumophilia
20. M. pneumoniae
21. C. pneumoniae
22. Coxiella burnetii
23. C. psittaci
24. M. tuberculosis
25. Flu B #1
26. Flu B #2
27. Staph PVL
28. Flu A #2
29. Flu A #3
30. S. pneumoniae#1
31. S. pyogenes#1
32. S. aureus (Nuc)
33. Aspergillus 28S
34. Flu A H12009
35. Flu A H3
36. Legionella species#1
37. H. influenzae #1
38. Enterovirus Br
39. M. pneumoniae #2
40. B. pertussis IS481
41. Parechovirus
42. P.jiroveci #1
43. RSV #3
44. HCoV OC43
45. Rnase P IC
46. HPIV 1 #2
47. HPIV 3 #3
48. Rhinovirus #2
49. HSV#1
50. HSV#2
51. HSV#3
52. HSV type 1
53. HSV type 2
54. EBV#1
55. EBV#2
56. VZV#1
57. VZV#2
58. CMV#1
59. CMV#2
60. BK#1
61. BK#2
62. BK/JC
63. Aspergillus 28S
64. Measles#1H
65. Measles#2 N
66. Legionella spp # 5a
67. Tamiflu S
68. Tamiflu R
69. IS481#2
70. L. pneumophilia #2
71. S. pneumoniae #2
72. H. influenzae #2
73. S. pyogenes# 2
74. N. meningitidis
75. Mec A
76. S. aureus (Nuc)
77. TB#2
78. TB#3
79. P.jiroveci #2
80. P.jiroveci #3
81. MS2 IC
82. EVD68
83. Acanthamoeba #1
84. Acanthamoeba #2
85. Fusarium #1
86. Fusarium #2
87. A. fumigatus new
88. B19
89. MERS #1
90. MERS #2
91. MERS #3
92. Leptospirosis #1
93. Legionella spp # 6a
94. Legionella species #2
95. Legionella species #3
96. Legionella spp # 4a

TaqMan® Array Cards: Process

5 – 10 Minutes

52 Minutes

Load

Spin

Seal

Run

20µL NA
25µL Master Mix
(Fast Virus 1 step)
55µL Water

1200 rpm / 2 mins

50°C	5 min	(RT)
95°C	20 sec	
95°C	1 sec	X 45
60°C	20 sec	

Approach to diagnostic testing

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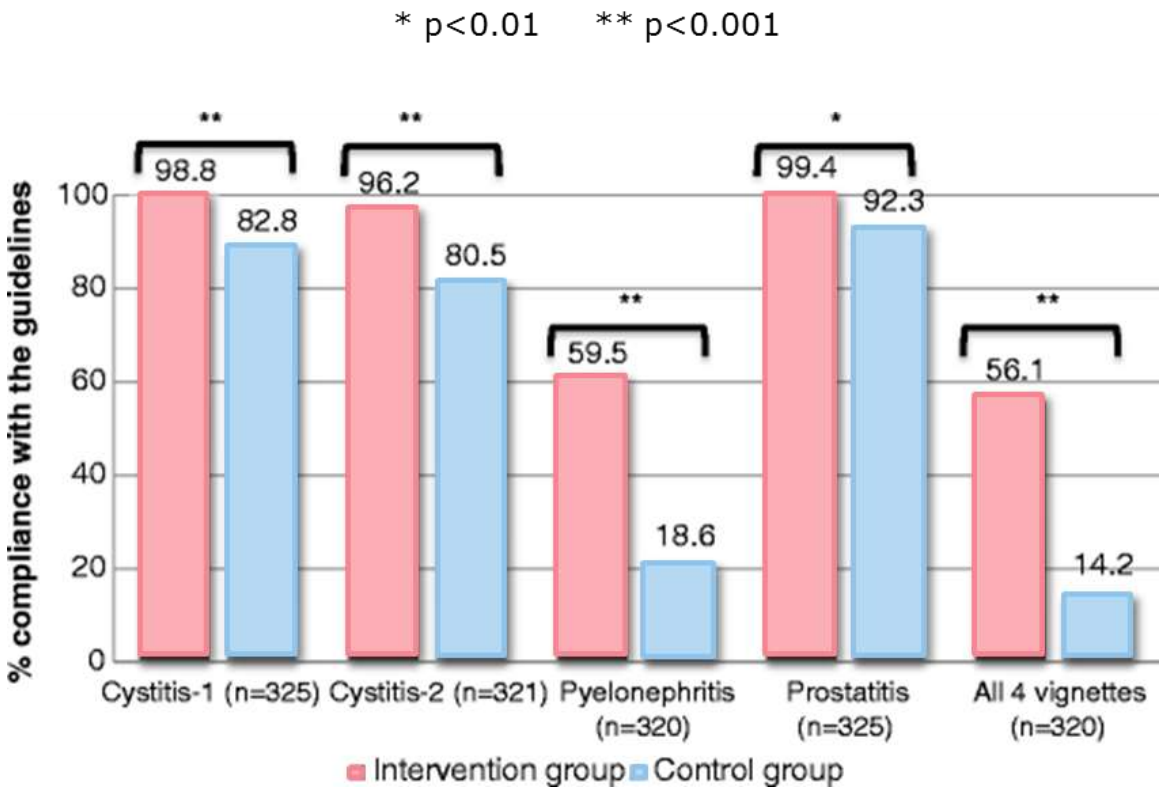
Selective antibiotic reporting

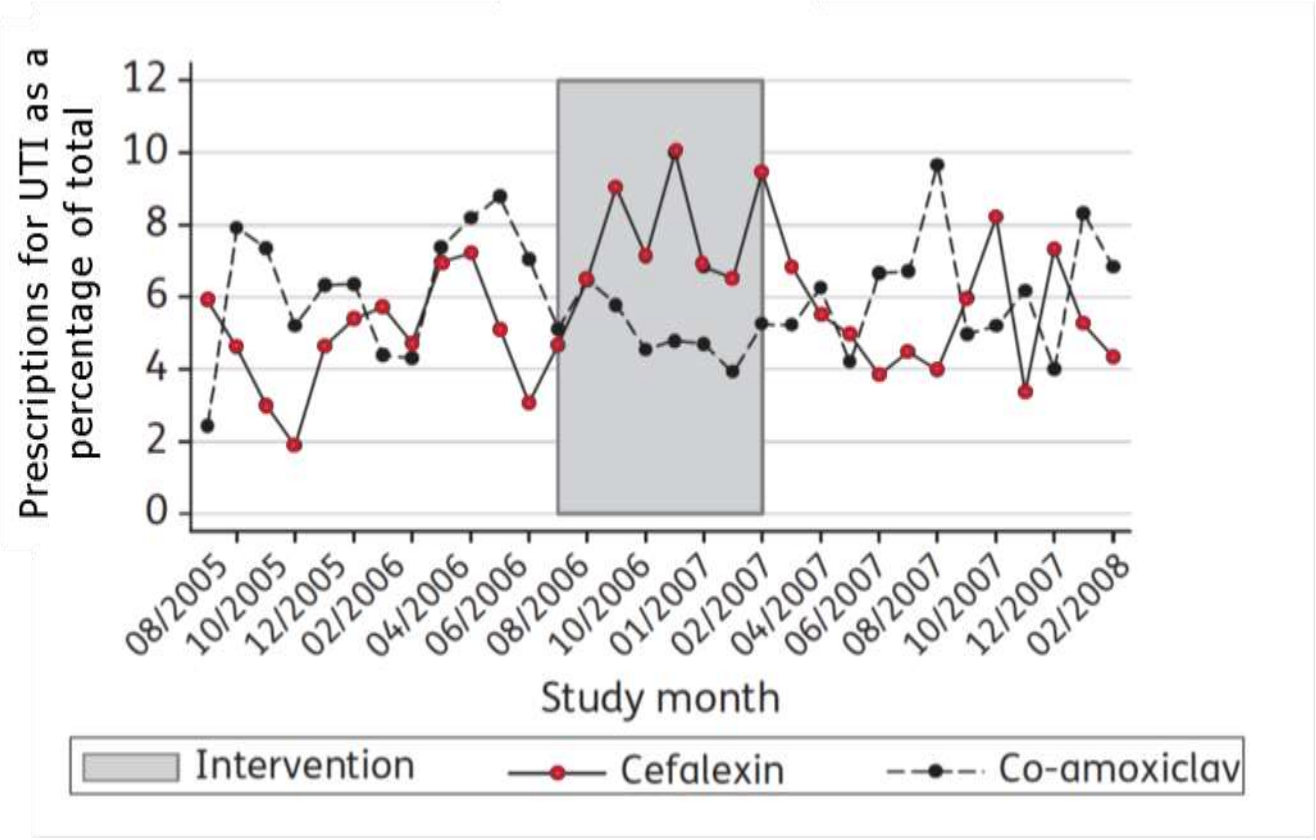
Clinical case histories presented to GPs



Coupat C et al. *Eur J Clin Microbiol Infect Dis* 2013; 32: 627–36

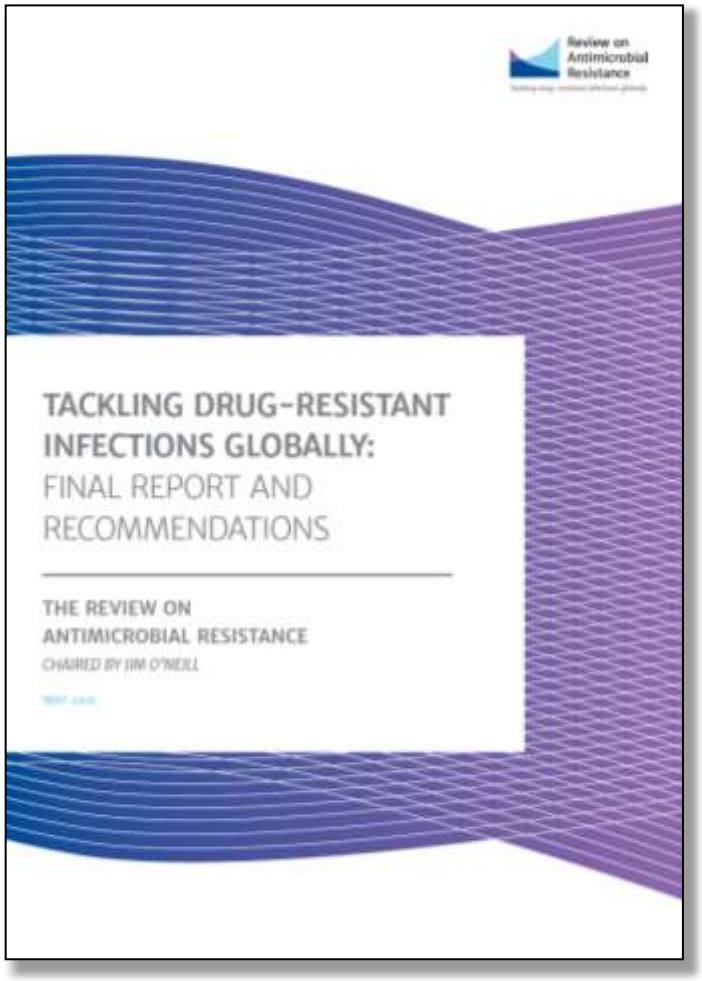
Selective antibiotic reporting

Change in reported antibiotic susceptibilities and impact on GP prescribing



McNulty CAM et al. *J Antimicrob Chemother* 2011; 66: 1396–1404

O'Neill update July 2019



10 areas, 29 recommendations

Progress in:

- R&D and investment in AMR
- Early development of new compounds

Lack of progress in:

- Big Pharma engagement and investment
- Diagnostics