Public Health Ontario | Santé publique Ontario

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https://youtu.be/ltyEyJcvEOE

Please scroll down this file to view a copy of the slides from the session.

Microbiology in Resource Limited Settings: Current practice, challenges and future directions

Public Health Ontario PHO Microbiology Rounds
13th October 2022

Dr Marta Gonzalez Sanz

Dr Arjun Chandna

Dr Sakib Burza

MORU Tropical Health Network

MEDECINS SANS FRONTIERES

Who we are…

- All physicians with extensive experience working in Low Resource Settings
- Two microbiologists/ID physicians, one generalist
- All currently work either with or alongside Médecins sans Frontières
- All interested in improving access to microbiology services across the Global South

Who are MSF?

- Doctors Without Borders/Médecins sans Frontières (MSF) is a private international association. The association is made up mainly of doctors and health sector workers and is also open to all other professions which might help in achieving its aims
- Médecins Sans Frontières provides assistance to populations in distress, to victims of natural or man-made disasters and to victims of armed conflict. They do so irrespective of race, religion, creed or political convictions
- Médecins Sans Frontières observes neutrality and impartiality in the name of universal medical ethics and the right to humanitarian assistance and claims full and unhindered freedom in the exercise of its functions

What does MSF do?

- Work in > 70 countries across the world
- Focus is emergency response, but these can be protracted crises (South Sudan/DRC) or rapid deployments (Ebola)
- Also focus on neglected populations (NTDs, HIV/AIDS)
- Services range from health mobile clinics to specialised hospitals
- Access to microbiology across this spectrum is extremely limited, and generally only where proximity to pre-existing providers (eg India) exist
- MSF has identified ABR as a wicked problem, and is working on solutions

What is the current scenario?

- Antimicrobial resistance represents a threat to global health-care systems
- All-age death attributable to AMR 27.3/100,000 in western sub-Saharan Africa[1]
- Serious data gaps in many LRS
- A study into sepsis in a neonatal unit in the Democratic Republic of the Congo found that nearly 75% of all isolates were resistant to WHO-recommended antibiotics[2]

[1] Global burden of bacterial AMR in 2019: a systematic analysis; Lancet, volume 399, Issue 10325

2 Etiology of early-onset neonatal sepsis and antibiotic resistance in Bukavu, Democratic Republic of the Congo.*Clin Infect Dis.* 2021; **73**: e976-e980

How does this impact Low Resource Settings?

- Low-resource settings (LRS) struggle to diagnose and effectively treat bacterial pathogens - empirical treatment is the standard of care
- Quality and coverage of clinical bacteriology laboratories in LRS are complicated by a lack of infrastructure and expertise
- In nearly all MSF/LRS laboratory settings, quality assurance procedures, skilled personnel, laboratory supplies, and adequate and functioning equipment are all in short supply

What is the current scenario?

- Rolling-out of clinical bacteriology laboratories in LRS raises numerous challenges, including procurement constraints, product stability and availability of qualified personnel
- Automated systems are restricted due to their high costs and high maintenance requirements
- Molecular-based methods for identification and antibiotic resistance testing are too costly and not yet ready to replace conventional methods for antibiotic susceptibility testing
- Whole genome sequencing (WGS) is not yet applicable in routine diagnostic use for LRS

What do we need to consider – question:

A: Clinical bacteriology laboratory in LRS should be patient-directed and guided by clinical reality

B: Services should be operated and managed by lab technicians who are non-experts in microbiology

C: Services should be well-conceived, cost-effective and built-for-purpose, not an “entry-level” version of its counterpart in high resource settings

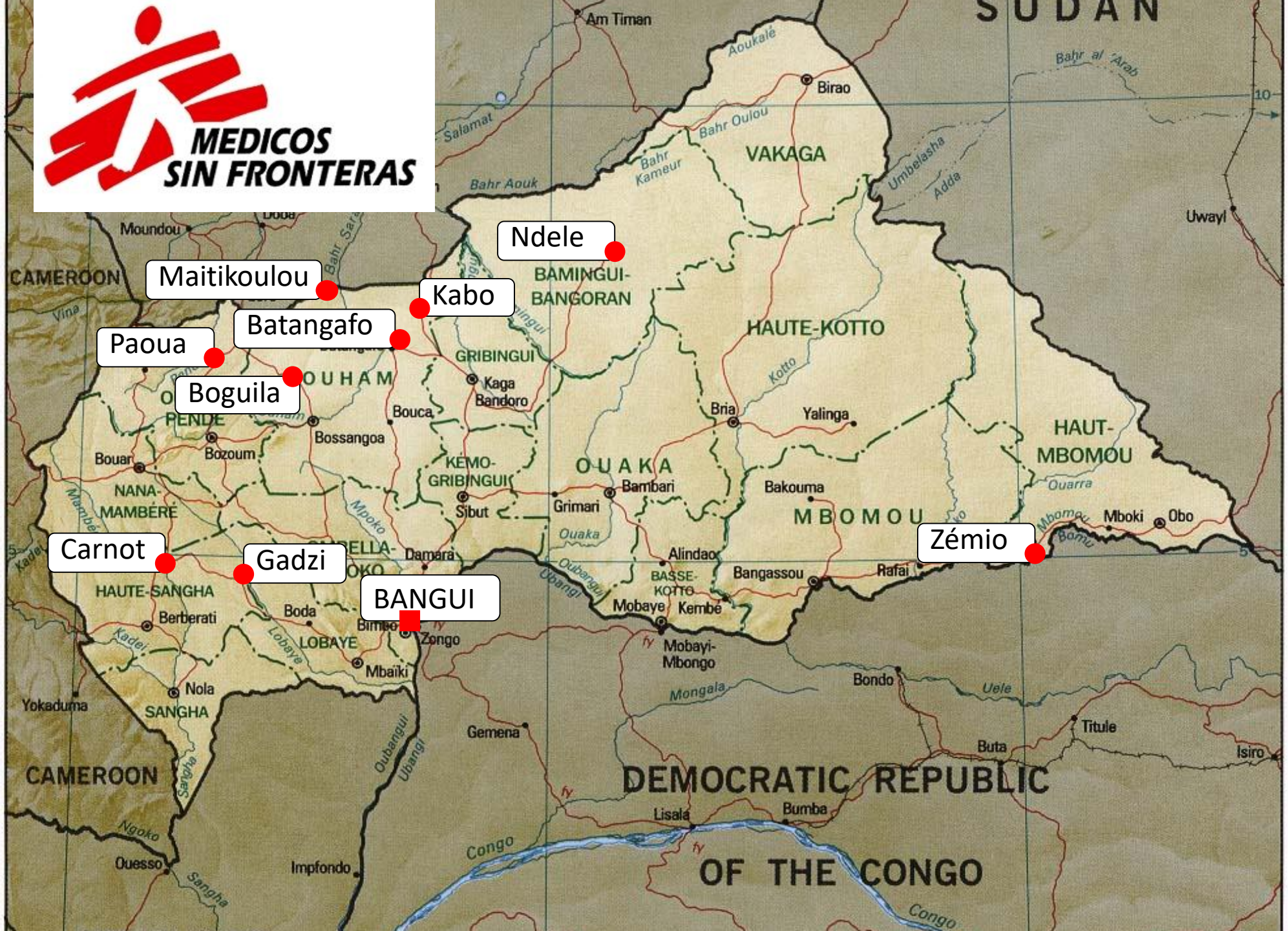
D: All of the above

Can high-quality clinical bacteriology can be implemented in the most remote, challenging, and underserved areas of the world to improve treatment and surveillance of antimicrobial resistant infections?

Objectives of the presentation

- Describe the current use of microbiology in resource limited settings
- Identify the challenges and pitfalls of introducing microbiology services in such settings.
- Recognise the laboratory governance issues and its impact on good microbiology practice in such settings.
- Appreciate their potential roles in supporting the expansion of microbiology services in resource limited settings
- Have fun!

Have you worked in resource limited settings?


MEDICOS SIN FRONTERAS
Ndele
Maitikoulou
Kabo
Batangafo
Paoua
Boguila
Carnot
Gadzi
BANGUI
Zémio
SUDAN
CAMEROON
VAKAGA
BAMINGUI-BANGORAN
HAUTE-KOTTO
GRIBINGUI
OUHAM
OUHAM-PENDE
KEMO-GRIBINGUI
OUAKA
HAUT-MBOMOU
MBOMOU
NANA-MAMBERE
HAUTE-SANGHA
LOBAYE
SANGHA
BASSE-KOTTO
CAMEROON
DEMOCRATIC REPUBLIC OF THE CONGO
Am Timan
Birao
Uwayl
Moundou
Kaga Bandoro
Bouca
Bossangoa
Bozoum
Bouar
Bria
Yalinga
Bambari
Grimari
Sibut
Bakouma
Mboki
Obo
Damara
Alindao
Bangassou
Rafai
Berberati
Boda
Mbaiki
Nola
Yokaduma
Zongo
Mobaye
Kembé
Mobayi-Mbongo
Bondo
Gemena
Titule
Buta
Isiro
Lisala
Bumba
Impfondo
Ouesso
Aoukalé
Bahr al 'Arab
Bahr Oulou
Bahr Kameur
Bahr Aouk
Umbelasha
Adda
Salamat
Vina
Kotto
Ouarra
Mbomou
Bomu
Mambéré
Mpoko
Ouaka
Kadei
Lobaye
Sangha
Oubangui
Ubangi
Mongala
Uele
Ngoko
Congo


MEDECINS
SANS FRONTIERES
STOP
GANGA SO AYEKE
NA MA PEPE


MINISTERE DE LA SANTE PUBLIQUE ET DE LA POPULATION
CENTRE DE SANTE
DE KABO
MEDECINS
SANS FRONTIERES


SANTE
INFANTILE
FAMILIALE

Is it possible to do quality microbiology in this setting?

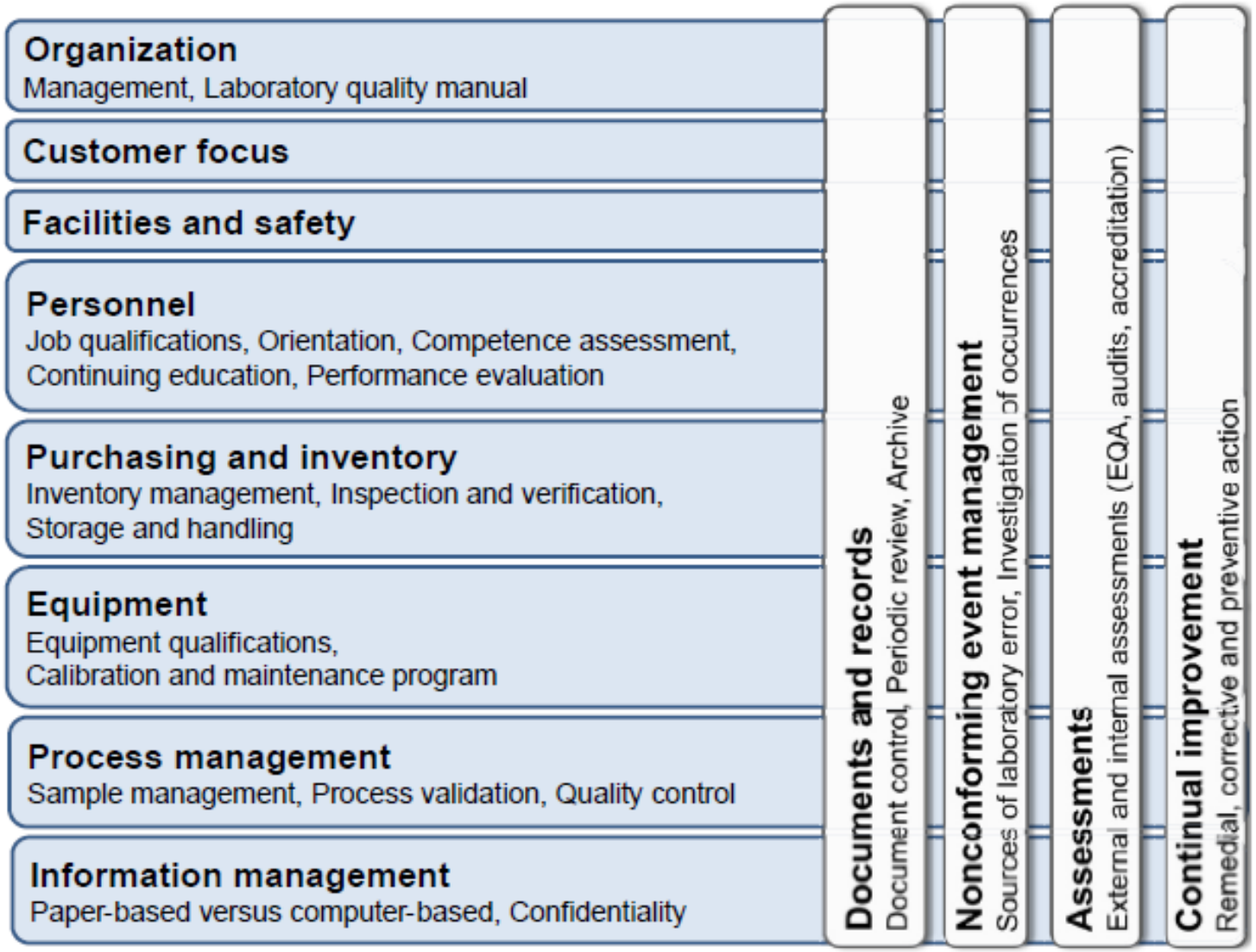
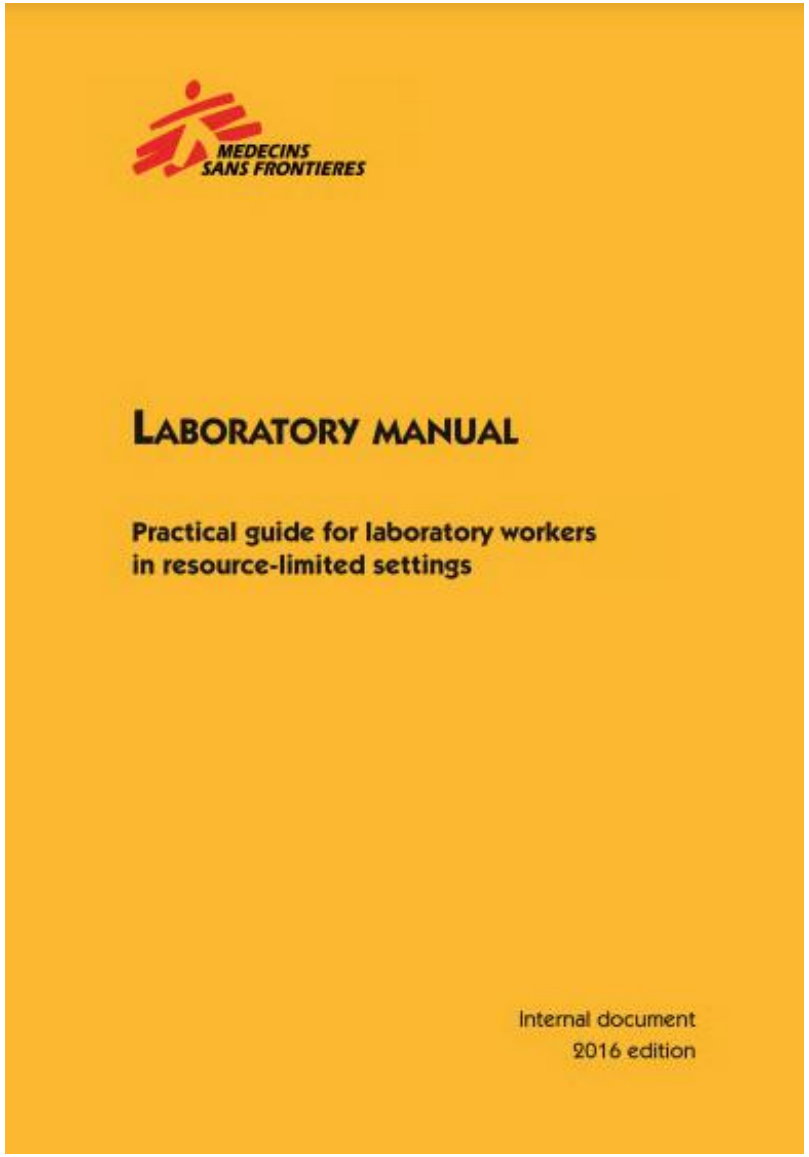
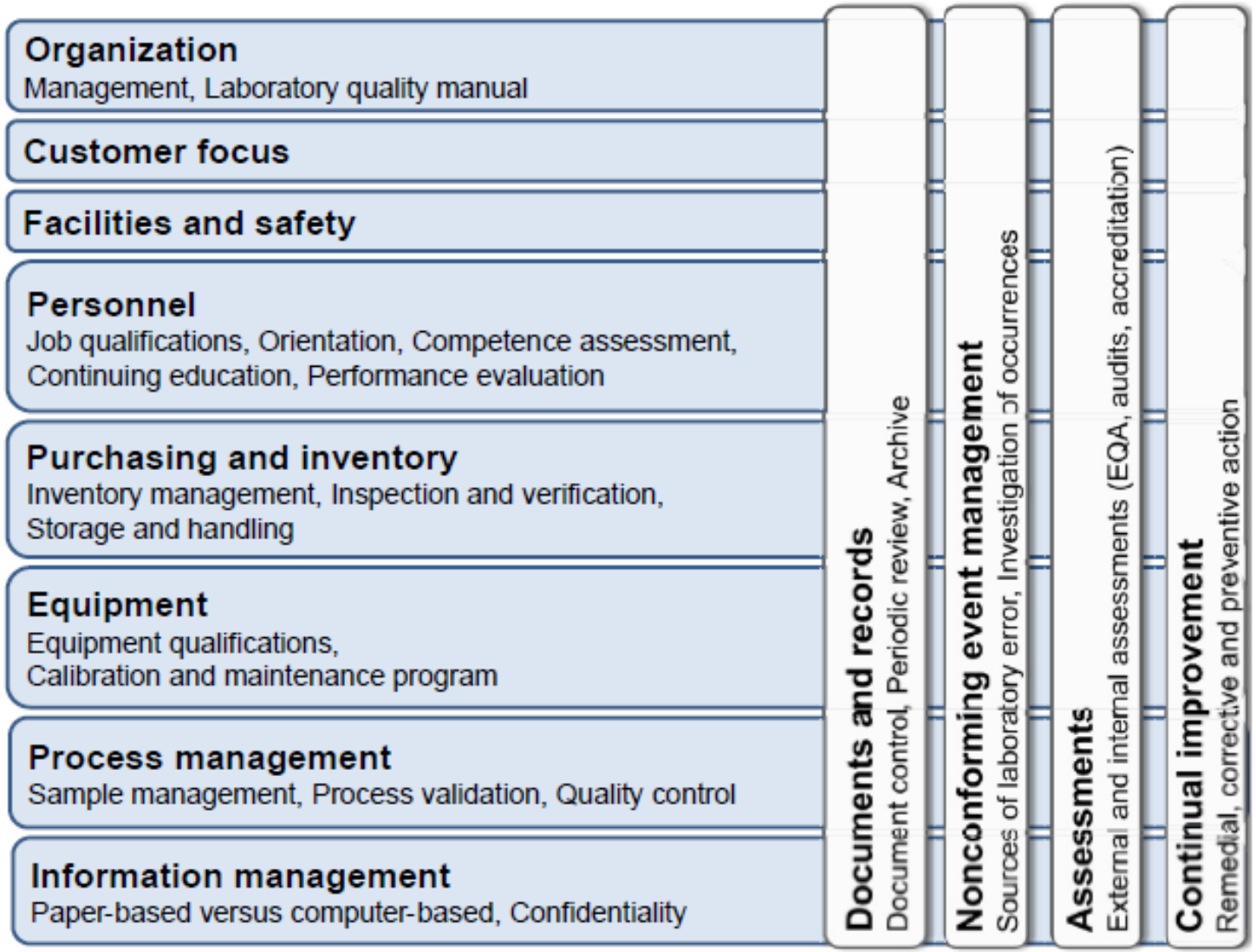


Fig. 1. Twelve quality system essentials of CLSI document QMS01-A4: Quality Management System: A Model for Laboratory Services [7]. General themes displayed horizontally, transversal themes vertically.

Sayed_Lancet_2018 Wertheim_ClinMicroInf_2021 Barbe_ClinMicroInf_2017



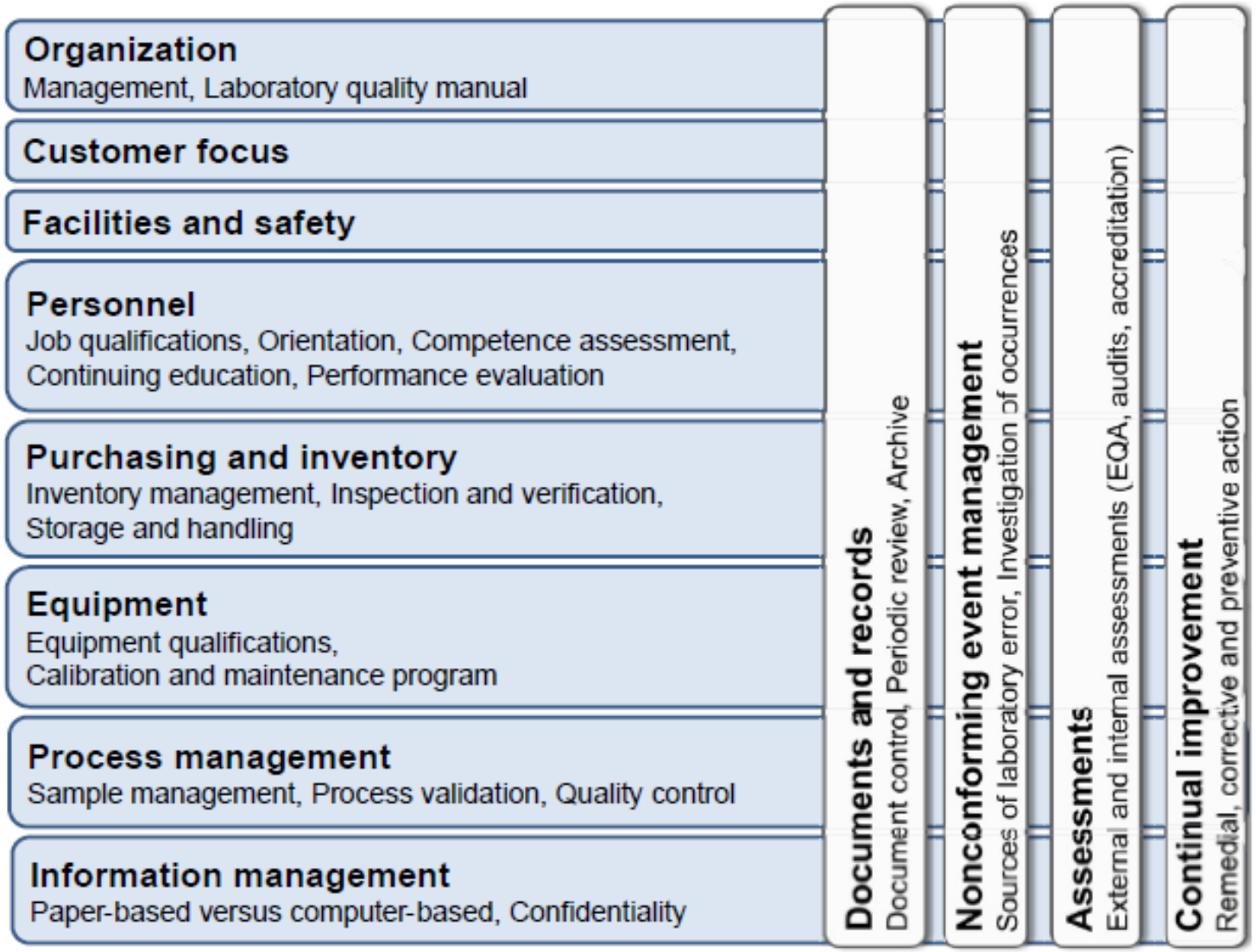
Sayed_Lancet_2018



Wertheim_ClinMicroInf_2021

Barbe_ClinMicroInf_2017

Increasing retention
Task shifting and sharing
Short term visitor programme



Short term visitor programme

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Sayed_Lancet_2018 Wertheim_ClinMicroInf_2021 Barbe_ClinMicroInf_2017

Supply

Organization
Management, Laboratory quality manual

Customer focus

Facilities and safety

Personnel
Job qualifications, Orientation, Competence assessment, Continuing education, Performance evaluation

Purchasing and inventory
Inventory management, Inspection and verification, Storage and handling

Equipment
Equipment qualifications, Calibration and maintenance program

Process management
Sample management, Process validation, Quality control

Information management
Paper-based versus computer-based, Confidentiality

Documents and records
Document control, Periodic review, Archive

Nonconforming event management
Sources of laboratory error, Investigation of occurrences

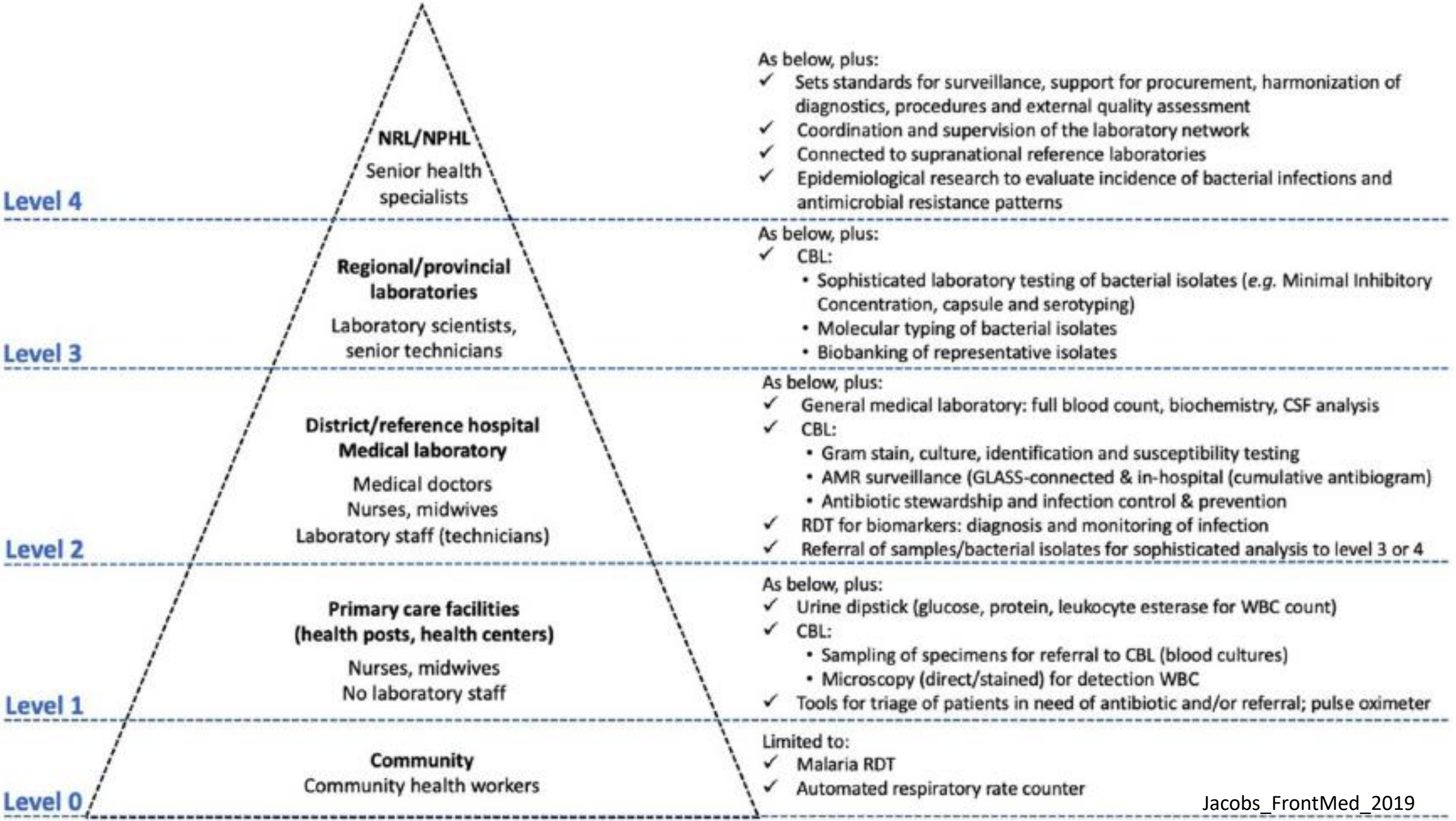
Assessments
External and internal assessments (EQA, audits, accreditation)

Continual improvement
Remedial, corrective and preventive action

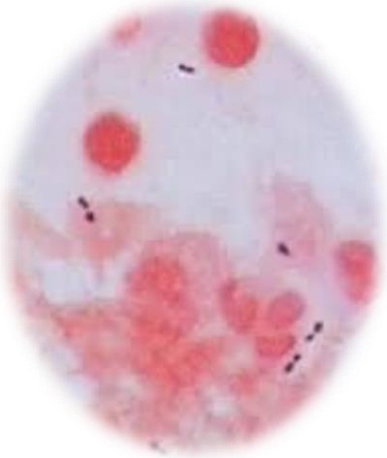
Sayed_Lancet_2018

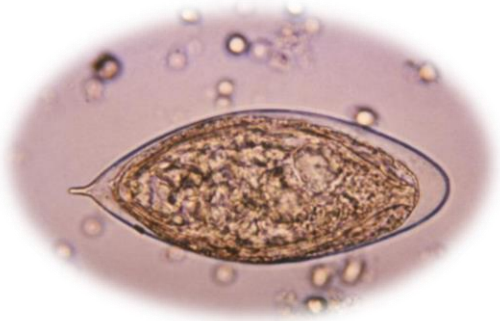
Wertheim_ClinMicroInf_2021

Barbe_ClinMicroInf_2017

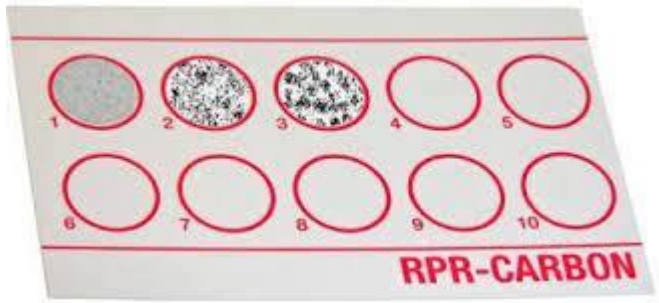


Jacobs_FrontMed_2019





- ✓ General medical laboratory: full blood count, biochemistry, CSF analysis
- ✓ CBL:
  - Gram stain, culture, identification and susceptibility testing
  - AMR surveillance (GLASS-connected & in-hospital (cumulative antibiogram)
  - Antibiotic stewardship and infection control & prevention
- ✓ RDT for biomarkers: diagnosis and monitoring of infection
- ✓ Referral of samples/bacterial isolates for sophisticated analysis to level 3 or 4



Case study

- 20F
- Re-admitted during malaria season
- Persistent fever for 3 weeks
- Abdominal pain, no diarrhoea
- Treated for malaria as an outpatient one week ago

- On examination: T 39 C, unwell, abdominal pain, no guarding or rebound

- Test performed:
  - Malaria RDT: Positive
  - Widal test: Negative
  - Pregnancy test : Negative
  - WCC: requested, lab technician too busy

What do you think?

A. The patient has a new episode of malaria, I would treat with first line antimalarials (artemisinin combination therapy)

B. The patient has resistant malaria, I would treat with a second line of antimalarials (e.g. atorvaquone/proguanil)

C. I cannot rule out typhoid, I would treat for a new episode of malaria and typhoid

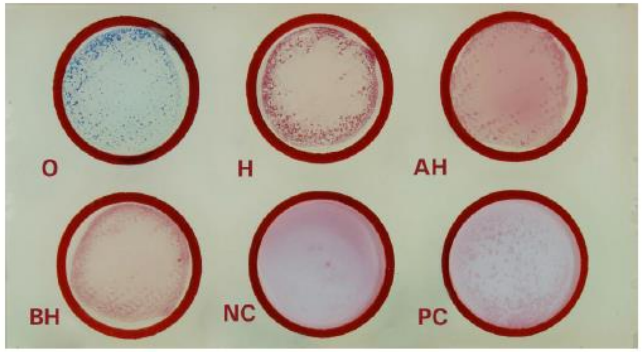
D. I am not sure about the diagnosis, I would treat malaria, start IV Ceftriaxone…I wish I had more tests available

MALARIA

- High prevalence area (severe malaria unlikely in adults, except for pregnant women)
- Malaria RDT detects antigen histidine-rich protein II (HRP2) and remains positive for up to a month after initial episode (median 2 weeks)
- Malaria thick and thin films should be requested

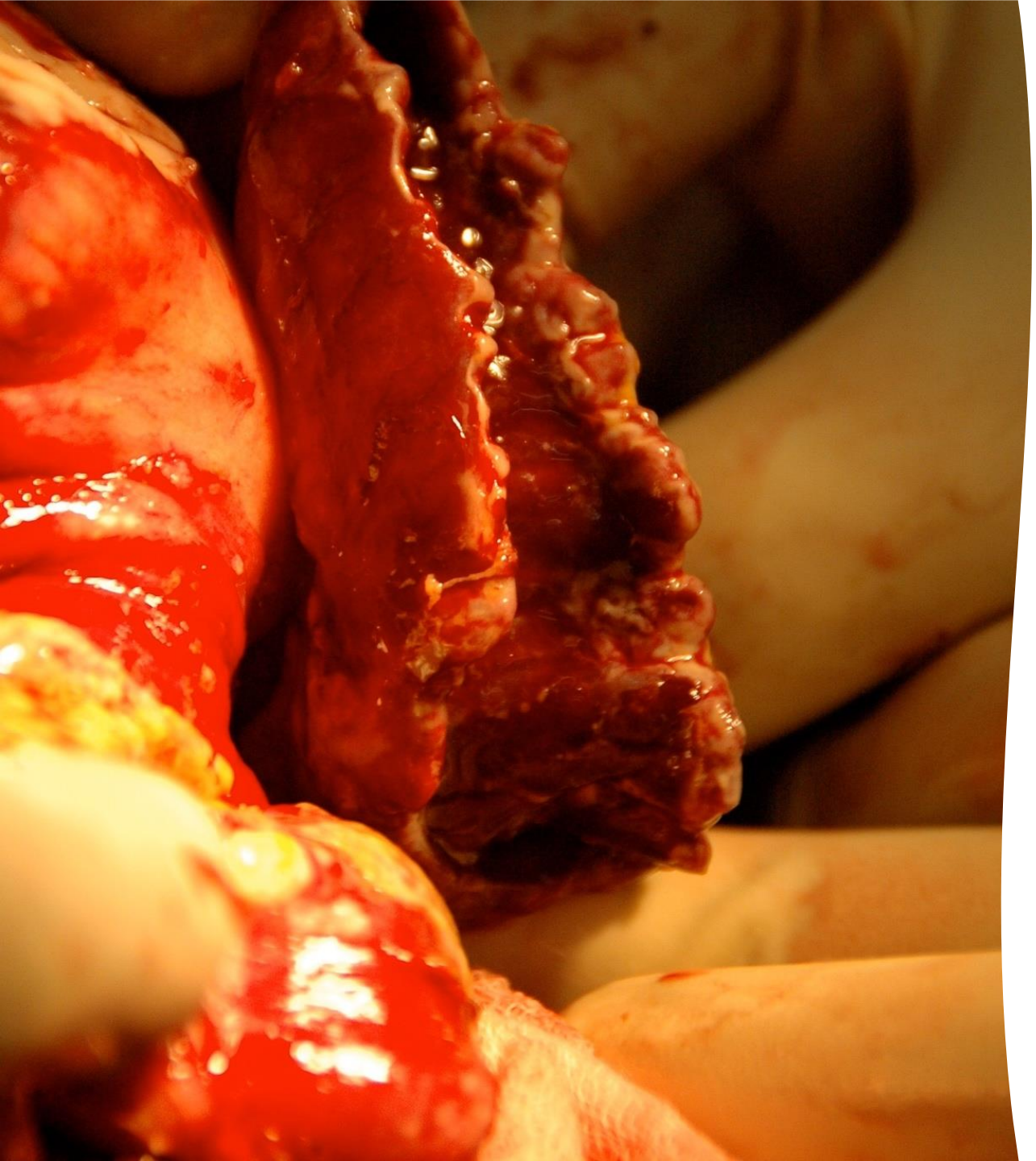
TYPHOID

- Widal test: agglutination test detects serum agglutinins (antibodies) against H and O antigens of *Salmonella typhi*
- Poor performance: Sensitivity 81.5%, Specificity 18.3%
- Still widely used in several countries



Dalrymple_MalariaJournal_2018

Mawazo_BMCResNotes_2019
Olopoenia_PostgradMedJ_2000



- Deterioration
- Abdominal guarding and rebound
- Taken to theatre…

It is not only about test availability but understanding:

- Correct indication
- Performance
- Interpretation

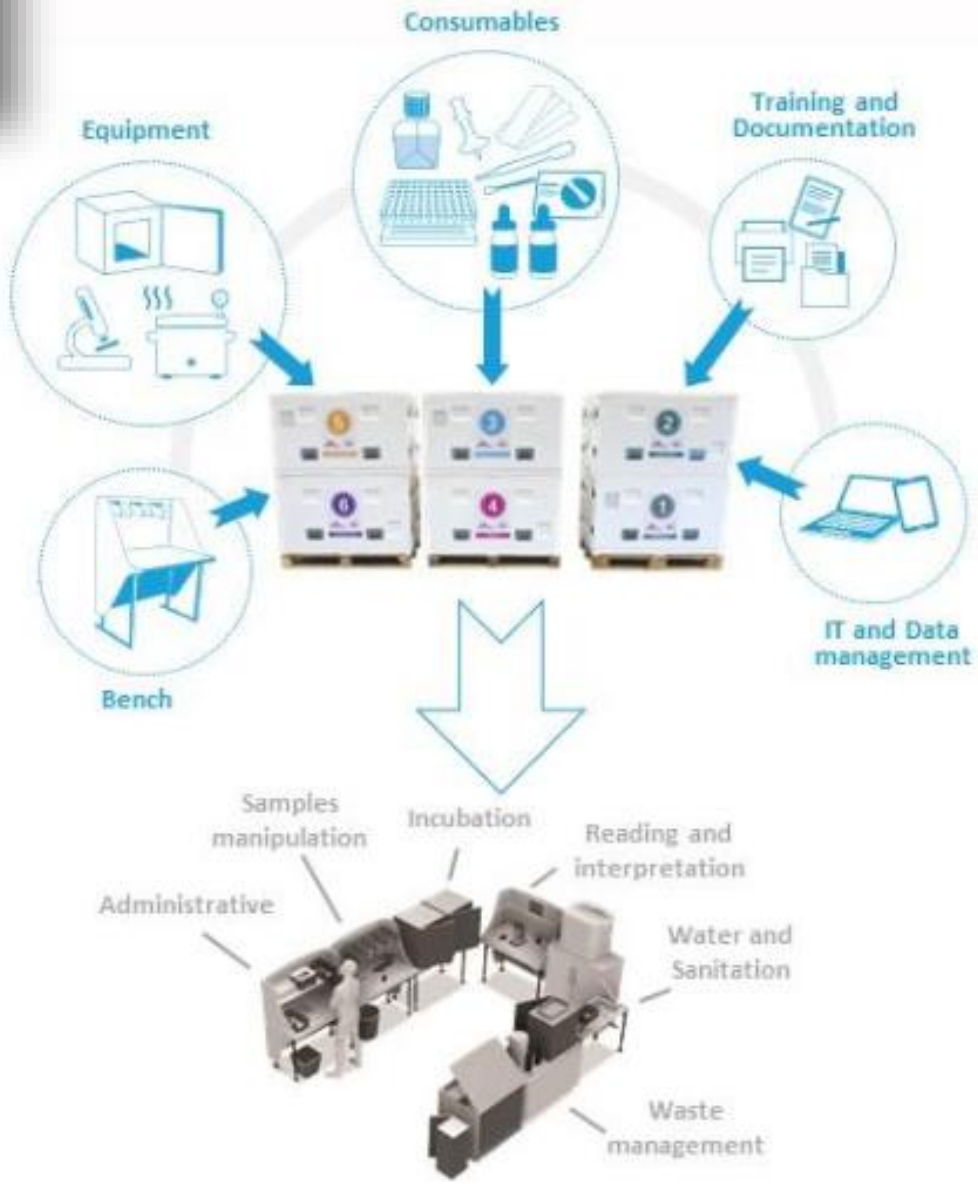
AMR taskforce

MEDECINS SANS FRONTIERES
DOCTORS WITHOUT BORDERS

Infection Prevention and Control

Antibiotic Stewardship

Diagnostics and Surveillance



15-20 m^2 to install the Mini-Lab (permanent structure, tent or container)

2 **days** to install or re-pack the Mini-Lab

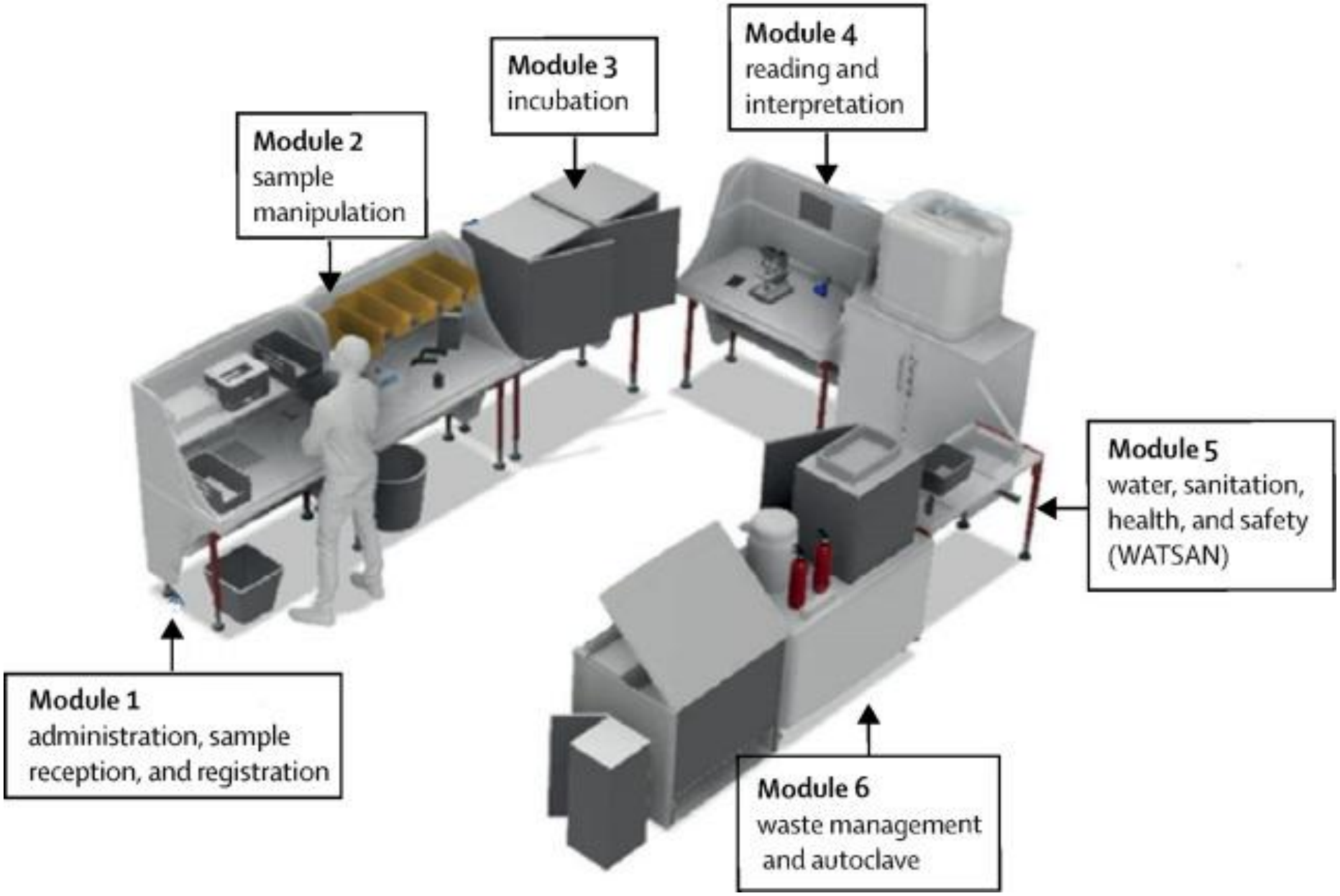
2/3 **Dedicated laboratory technicians** of which one is the supervisor (can be the same of other lab services)

20 **Days of on-site training** for the lab techs to be able to run the Mini-Lab

4-6 **Months** of initial onsite support and regular follow-up visits

10 - 20 **BCB / Day** (average & peak capacity until 30)

https://fondation.msf.fr/en/projects/mini-lab

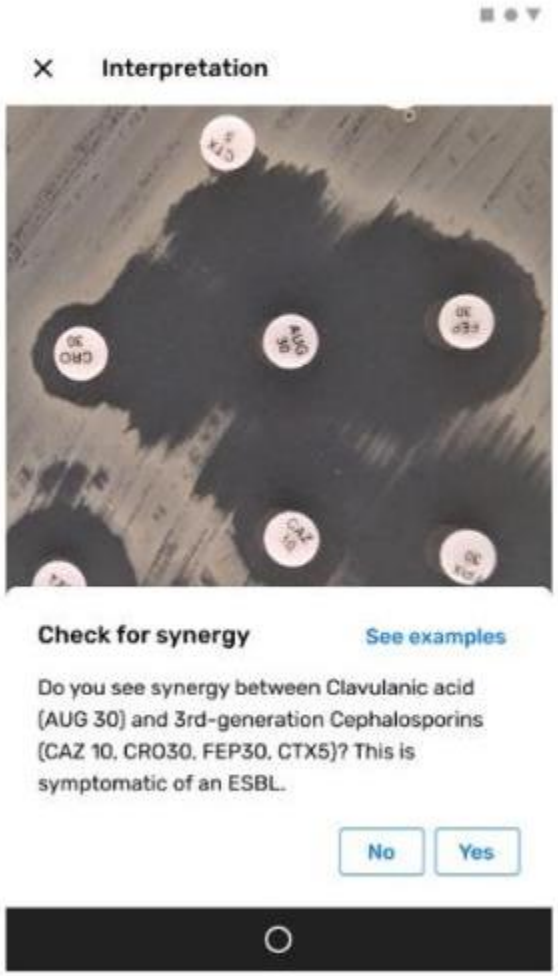

Module 4
reading and
interpretation
Module 3
incubation
Module 2
sample
manipulation
Module 5
water, sanitation,
health, and safety
(WATSAN)
Module 1
administration, sample
reception, and registration
Module 6
waste management
and autoclave

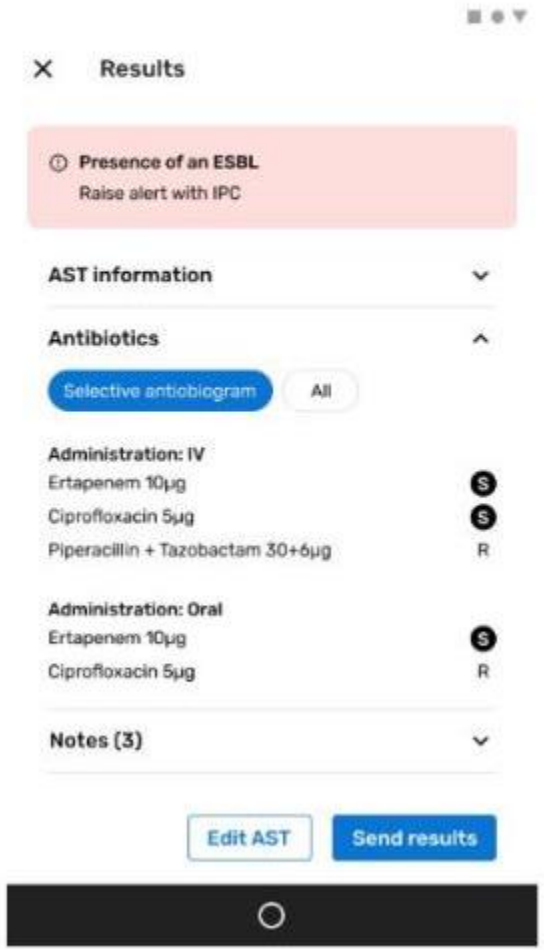
Antibiogo

1 - MEASURE EASILY
Take a picture of the petri dish, and measure inhibition zones for each antibiotic disc.

2 - GENERATE RESULTS
After image analysis, answer guided interpretation questions to generate AST result.

3 - SEND RESULTS
Ask for a peer's approval or share results directly with the clinician.



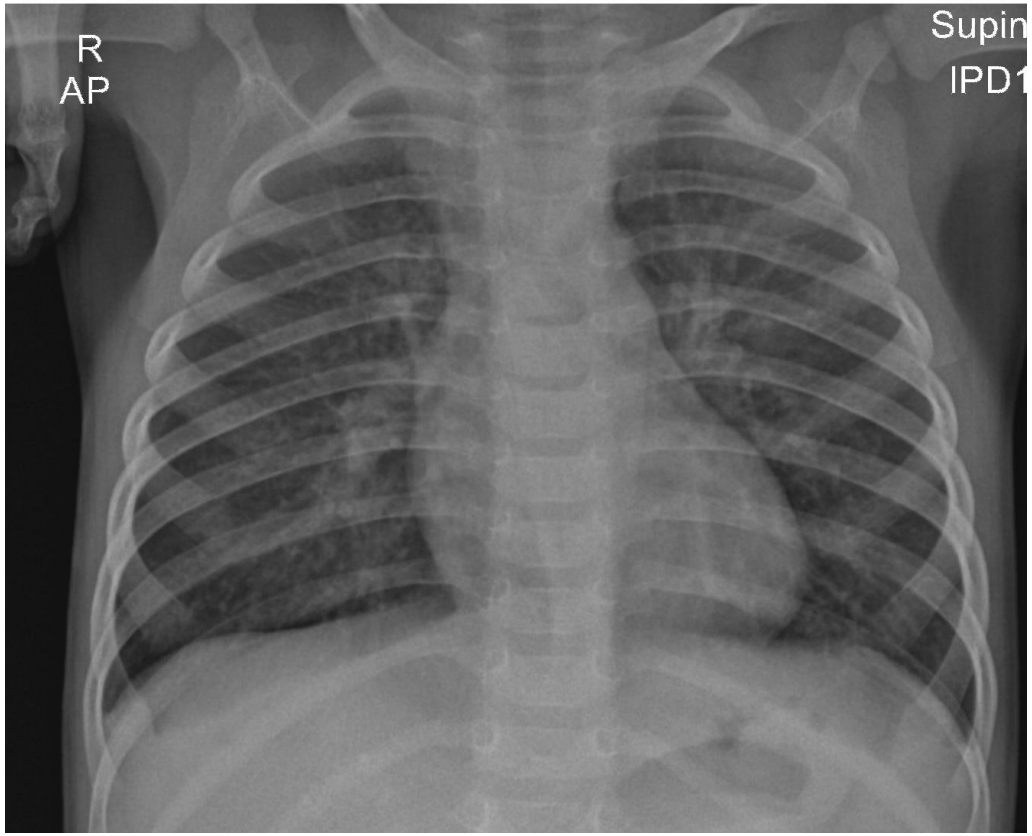


https://fondation.msf.fr/en/projects/mini-lab

Is it possible to do quality microbiology in resource limited settings?

Case study

- 19m boy; fever and cough for 7d
- Temp 38.1, HR 170, RR 40, SpO_2 99% (RA)
- O/E: bilateral crepitations
- Investigations
  - WCC 15.3 x 10^9 cells/L
  - Neutrophils 5.8 x 10^9cells/L
  - CRP 9 mg/L
  - UA = NAD



- D0 = admit, paracetamol, IV fluids, IV ampicillin
- D5 = still febrile, chest indrawing, not hypoxic, blood culture = NG

What would you do next?

A = Repeat blood/urine culture, continue ampicillin

B = Repeat blood/urine culture, abdominal/lung ultrasound, stop ampicillin, start ceftriaxone

C = Repeat blood/urine culture, abdominal/lung ultrasound, stop ampicillin, start meropenem

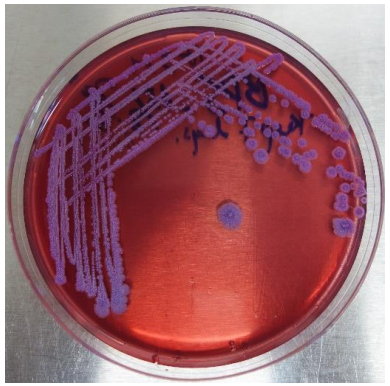
D = Repeat blood/urine culture, throat swab culture, abdominal/lung ultrasound, stop ampicillin, start ceftriaxone

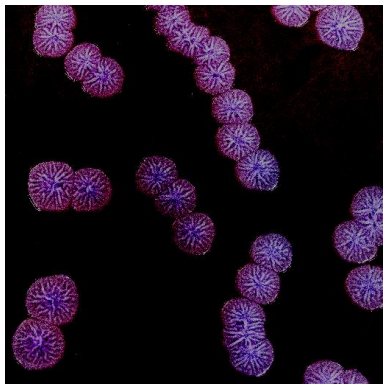
E = Repeat blood/urine culture, throat swab culture, add doxycycline

What would you do next?

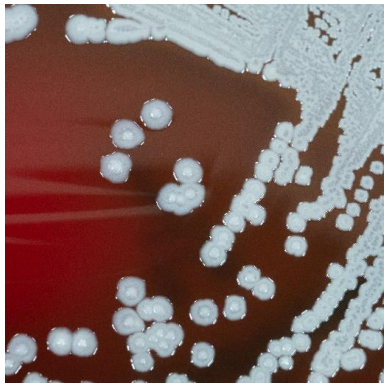
D = Repeat blood/urine culture, throat swab culture, abdominal/lung ultrasound, stop ampicillin, start ceftriaxone

- Throat swab culture grew *Burkholderia pseudomallei* after 24h
- Patient switched to ceftazidime; defervesced in 72h
- Completed 14d ceftazidime followed by 3m co-trimoxazole
- Well on follow-up

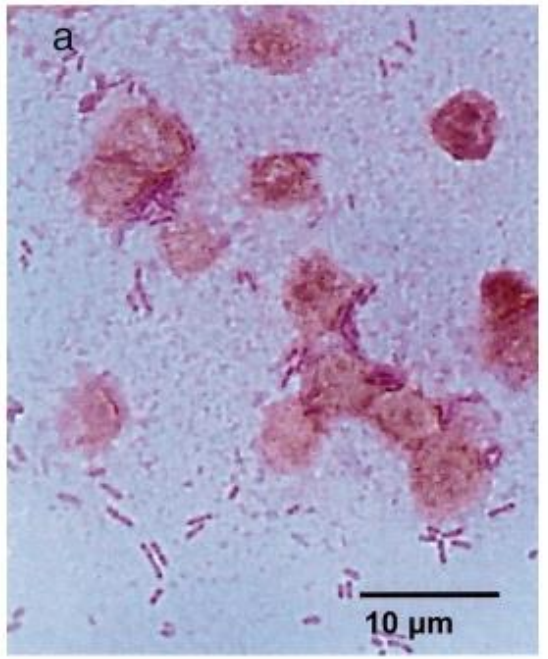




Ashdown agar after 72h incubation



Blood agar after 48h incubation



Gram stain of *B. pseudomallei* in a blood culture. 10th Edition, The Manual of Clinical Microbiology

J Antimicrob Chemother 2018; **73**: 509–516
doi:10.1093/jac/dkx414 Advance Access publication 24 November 2017

Journal of Antimicrobial Chemotherapy

Utilization of a clinical microbiology service at a Cambodian paediatric hospital and its impact on appropriate antimicrobial prescribing

Shivani Fox-Lewis[1,2]*, Sreymom Pol[1,3], Thyl Miliya[1,4], Nicholas P. J. Day[2,3], Paul Turner[1–4] and Claudia Turner[1–4]

Clinical / Education

- Daily infection consults
- Weekly educational rounds (interns)
- Twice weekly PICU rounds
- Antimicrobial e-guidelines (MicroGuide)
- Quarterly PPS/AMC and HAI reports
- Monthly BSI reports

Establish a culture that micro can be useful

- Diagnostic stewardship
- MDT working
- Partnership and flexibility
- Built-for-purpose

Microbiology Specimen Collection For AMR Surveillance in Children

Which samples should I send?

Sepsis or Severe febrile illness

For **all** patients:
Urine
Blood culture

For selected patients:
CSF
Other relevant cultures (e.g. pus, throat swab)
Malaria film
Viral workup (e.g. dengue)

Meningitis

For **all** patients:
Blood culture
Blood glucose
CSF if no contra-indications

For selected patients:
Malaria film
TB microscopy / culture
Viral workup (e.g. JEV)
Fungal workup

Severe pneumonia

For **all** patients:
Blood culture

For selected patients:
Sputum sample
- If productive cough (older children only)

Broncho-alveolar lavage
- If severe or intubated

Tracheal aspirate
- If intubated

When should I send a blood culture?

Always send a blood culture in these situations
Take the blood culture before the first dose of antibiotic

Sepsis
Dysregulated host response to infection
Features to alert suspicion ("red flags"):
- *Abnormal core temperature*
  < 36.0°C / > 38.5°C tympanic OR
  < 35.5°C / > 38.0°C axillary
- *Inappropriate tachycardia*
  <1y: ≥ 160 /min
  1-2y: ≥ 150 /min
  3-4y: ≥ 140 /min
  5y and above: ≥ 130 /min
- *Altered mental state*
  GCS < 15 OR
  Sleepiness, irritability, lethargy, floppiness
- *Reduced peripheral perfusion or prolonged capillary refill time*
  Cold feet or hands OR ≥3 sec

Severe febrile illness
In a children aged < 5 years
Fever (T > 37.5°C) plus ≥ 1 danger sign:
- *Unable to feed or drink*
- *Vomiting everything*
- *Lethargy*
- *Unconscious*
- *Convulsion*

Meningitis
Sudden onset fever (T >37.5°C) plus ≥ 1 feature of meningism:
- *Headache*
- *Neck stiffness*
- *Photophobia*
- *Kernig's sign positive*

Neonatal sepsis
Patient < 28 days old plus ≥ 1 of:
- *RR > 60*
- *T > 37.5°C or T < 35.5°C*
- *Respiratory distress*
- *Reduced movement*
- *Convulsion*
- *Poor feeding*

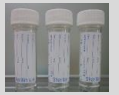
Severe pneumonia
Cough or dyspnoea plus ≥ 1 of:
- *Cyanosis*
- *O_2 saturation < 90%*
- *Severe respiratory distress*
- *Danger sign (see above)*

How should I send my sample?

Blood culture

1ml minimum volume
4ml maximum volume

CSF



Send 3 tubes
1ml CSF in each tube

General specimen pot

BAL / ETT aspirate
Pus
Sputum
Sterile fluids
(e.g. ascites, joint fluid)
Stool
Tissue / Biopsy
Urine

General swab

Ear, Eye, Throat
Genital, Skin, Wound

Remember to **clean** a wound before taking the swab

HOSPITAL LOGO

Microbiology contact details

ACORN

Improving Treatment and Outcomes for Melioidosis in Children, Northern Cambodia, 2009–2018

Arjun Chandna,[1] Moritz Bonhoeffer,[1] Thyl Miliya, Keang Suy, Sena Sao, Paul Turner

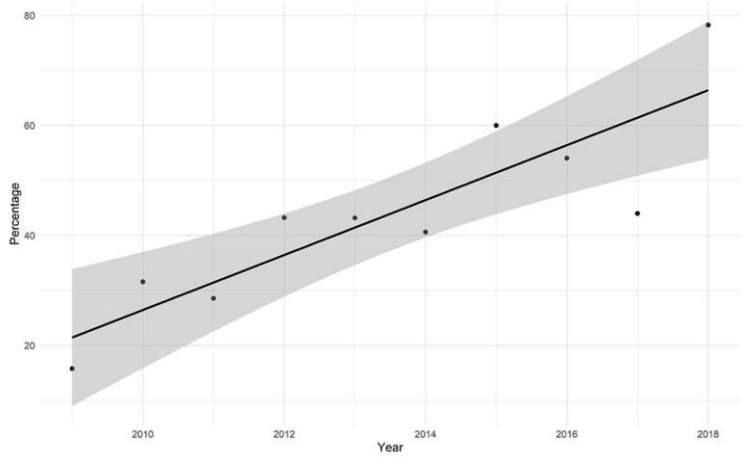
Emerg Infect Dis. 2021;27(4):1169-1172

2009
Manual BC
Gram / API
Disc AST

2018
Manual BC
MALDI-ToF
Disc AST

DIAGNOSTICS

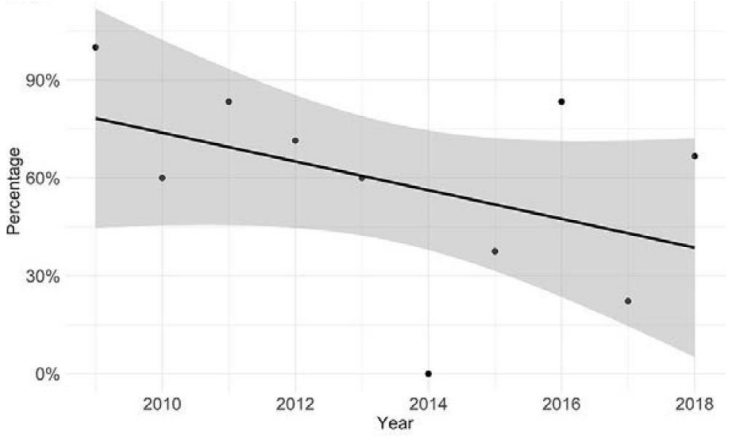
Proportion of patients with blood culture collected



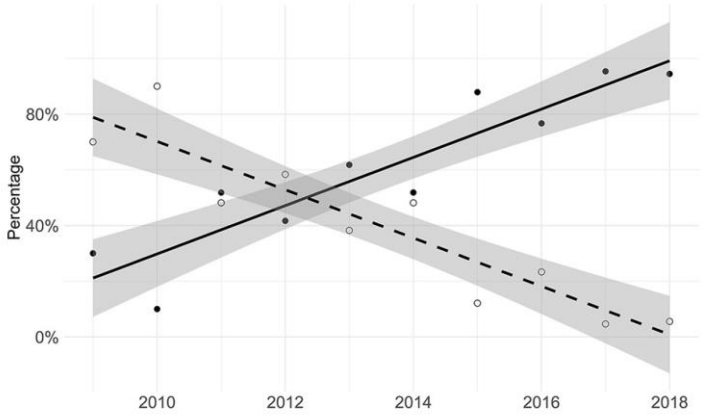
Sample	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Throat swab	1	1	1	0	0	0	1	2	15	10
Urine	0	0	0	0	0	0	0	1	5	10

OUTCOMES

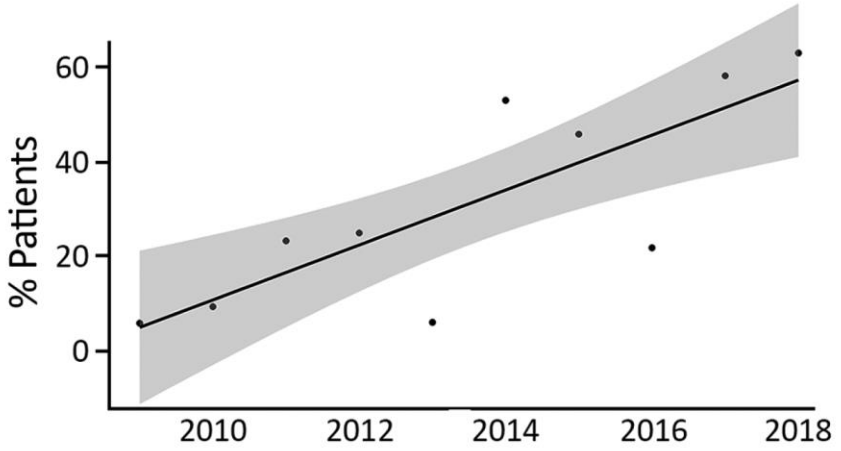
Mortality rate in bacteraemic patients



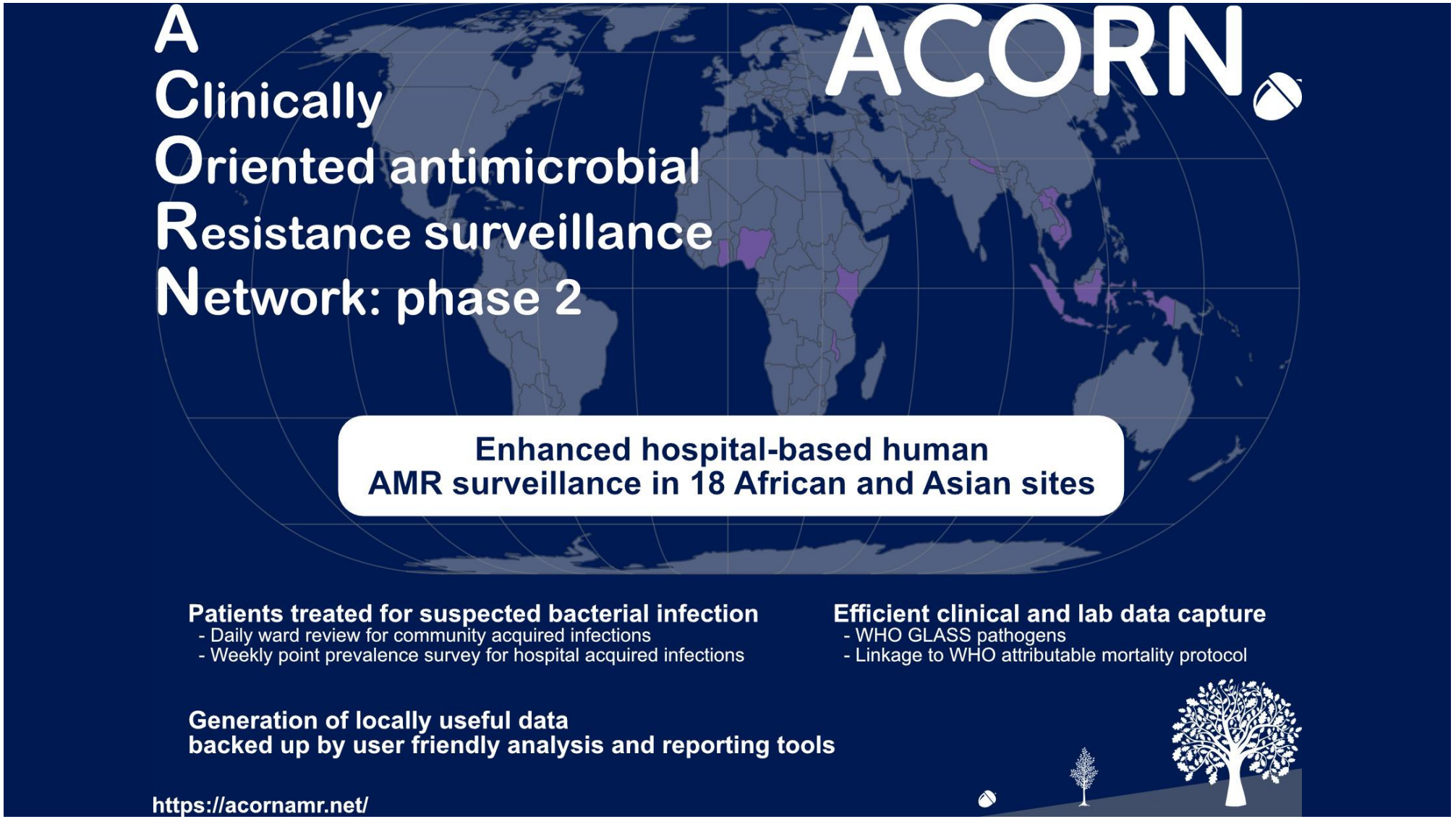
Proportion of patients on co-trimoxazole (solid line) vs. co-amoxiclav (dashed line) for eradication phase



Proportion of patients successfully completing 12 weeks eradication therapy



Local data for local use (acornamr.net)



Thank you

Any questions?