Diagnosis of *Helicobacter pylori* infections - an African perspective

Ebrahim Hoosien
Clinical Microbiology
Ampath Laboratory

H. pylori – Factors to consider…

Prevalence

Global and regional variance

Transmission associated with socioeconomic conditions

Bacterial clone diversity associated with different sequela of bacterial infection

Pathophysiology

Intimately adapted to human colonisation

Asymptomatic carriage might promote or aggravate other disease

Host genetic variances give differences in sequela of bacterial infection

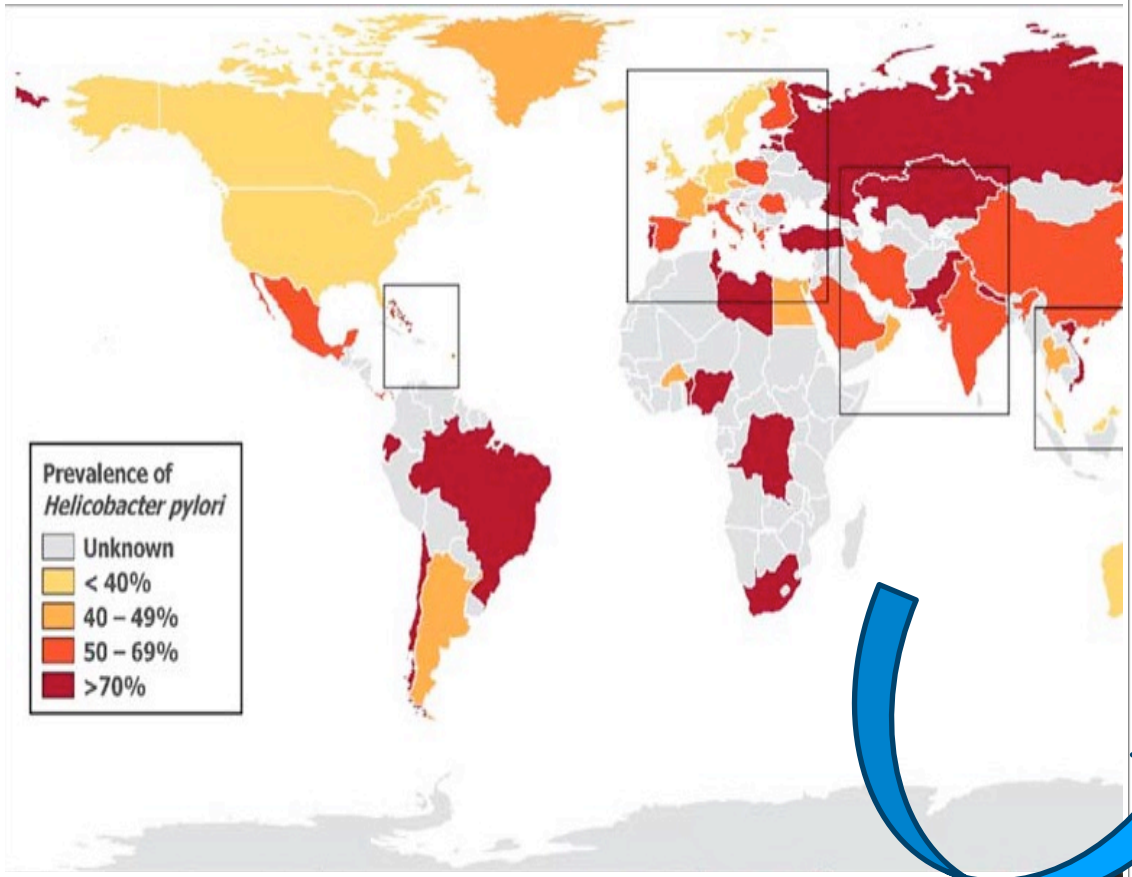
Antimicrobial susceptibility

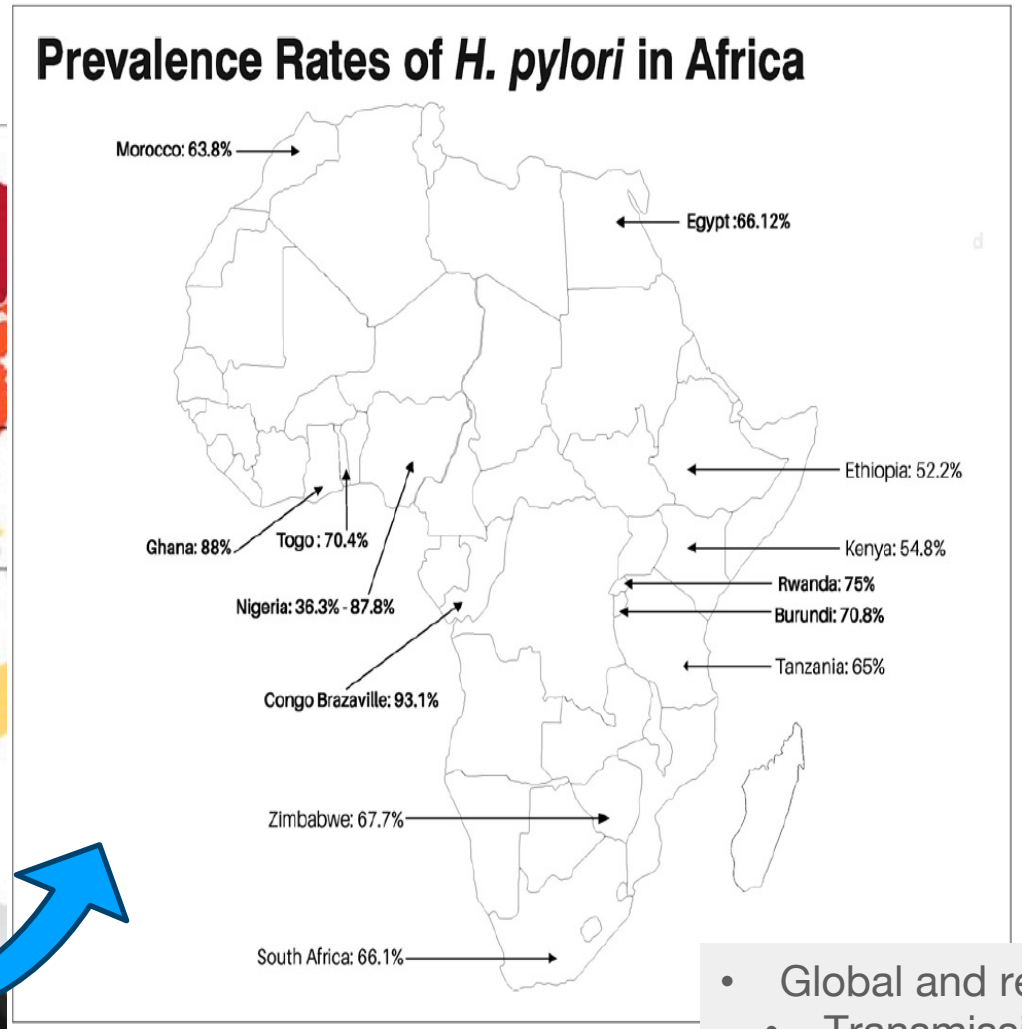
Multiple antibiotics required along with a PPI

Susceptibility testing algorithm differ based on regional resistance

Fastidious organism making bacterial isolation a challenge

Global and regional variance



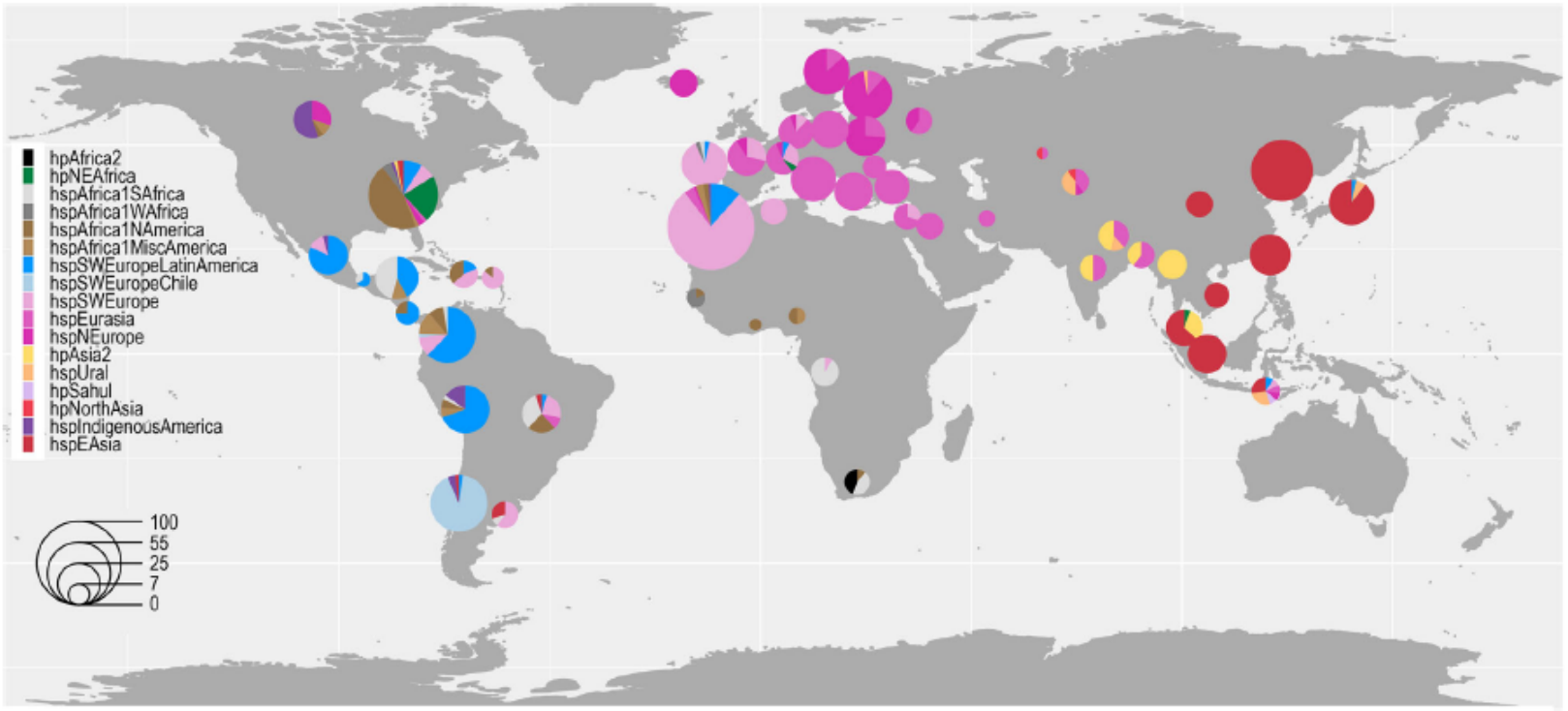


- Global and regional variance
- Transmission associated with socioeconomic conditions

Disease outcome of *H. pylori* infection

The *Helicobacter pylori* Genome Project: insights into *H. pylori* population structure from analysis of a worldwide collection of complete genomes

Thorell K et al. Nature Communications. 2023 Dec 1



Bacterial clone diversity associated with **different geography and gastric disease**

Over half the world's population is colonised with less than 2% with gastric cancer

H. pylori has co-existed with humans for more than 100,000 years

Disease outcome of *H. pylori* infection

Helicobacter pylori **patient isolates from South Africa and Nigeria differ in virulence factor pathogenicity profile and associated gastric disease outcome**

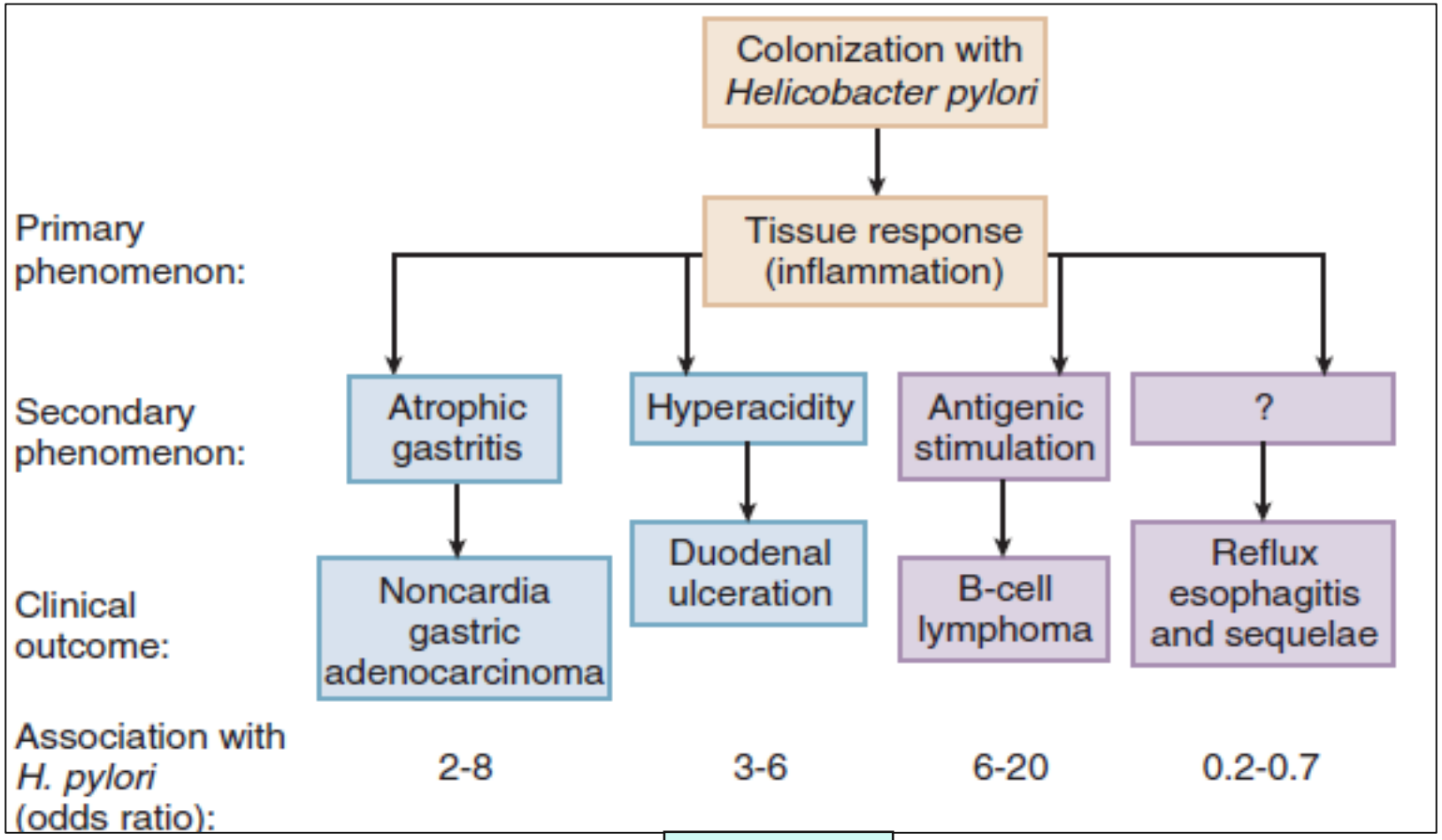
Palamides P, et al. Scientific Reports. 2020 Dec 1

- 220 isolates biopsy; 114 Isolates
- Different bacterial genotypes
  - hspWestAfrica subtype of hpAfrica1 dominant in Nigeria
  - hpAfrica2 strains higher in RSA

- Endoscopy findings visually :

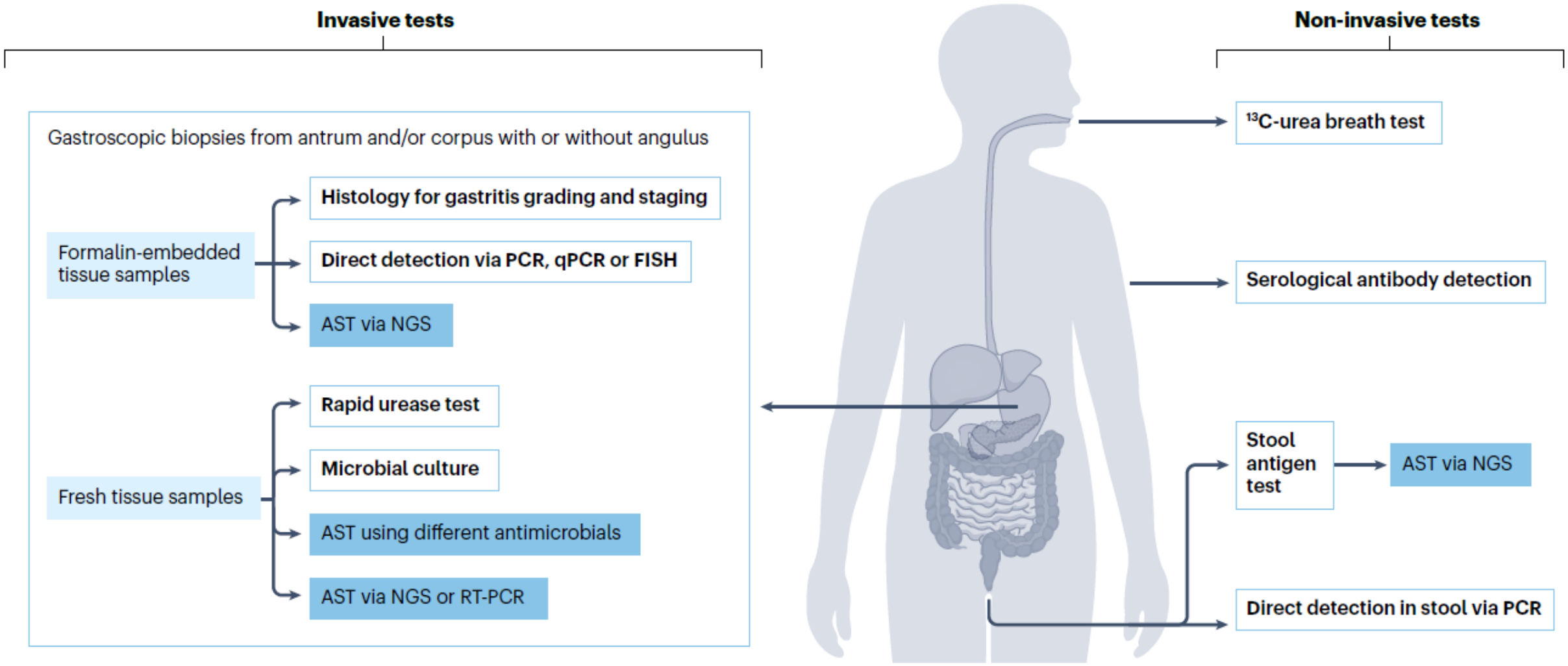
- Nigerian patients significantly more erosions

Disease outcome of *H. pylori* infection



? Africa

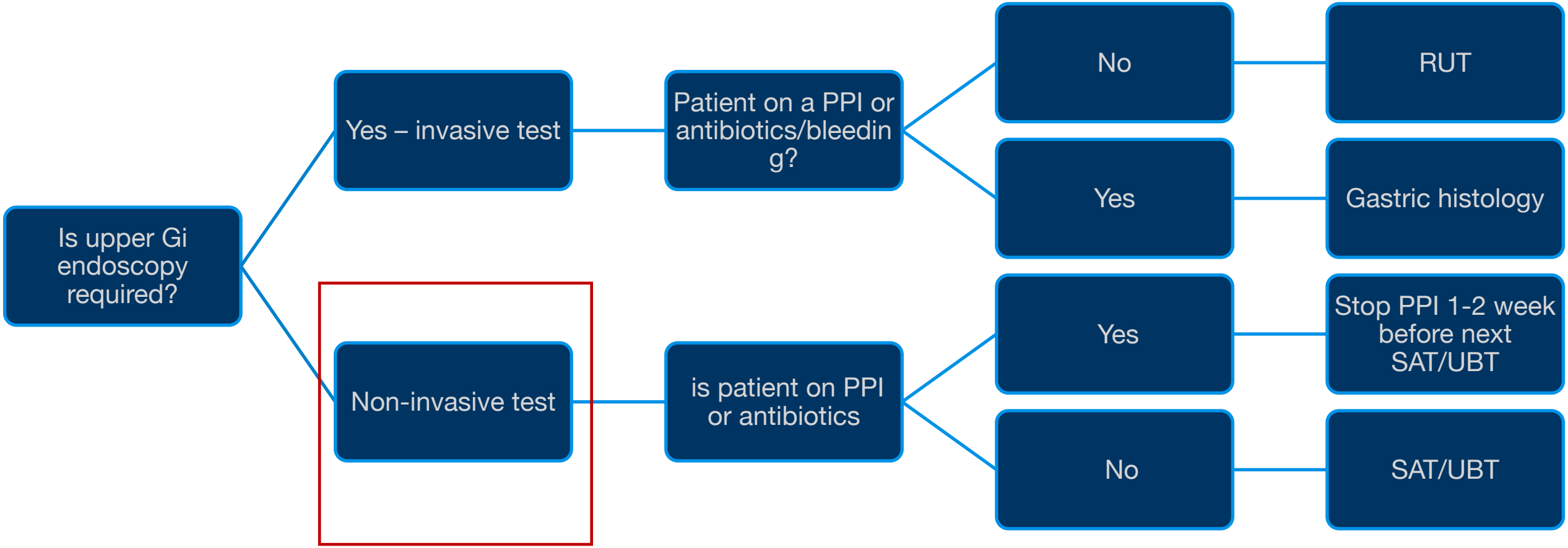
Diagnostic modalities



WGO CASCADES: Diagnostic tests for *H. pylori* according to resource level

Endoscopy-based and non-endoscopy based test	High resources	Intermediate resources	Low resources
Histology	Widely	Usually	Rarely
Commercial urease tests	Widely	Widely	Rarely
In-house urease tests	Widely	Widely	Widely
Culture	Many centres	Major centres	Rarely
PCR - biopsy	Major centres	Rarely	Rarely
Breath tests ^{14}C urea	Widely	Usually	Major centres
^{13}C urea	Usually	Major centres	Rarely
Stool antigen test	Usually	Usually	Major centres
Stool PCR	Major centres	Rarely	Rarely
Serology venous	Widely	Usually	Usually

Diagnostic pathways



African Helicobacter and Microbiota Study Group

Africa has low access to endoscopy and molecular based diagnostics

High prevalence of *H.pylori* infection

UBT and SAT are recommended – test and treat strategy

Stool antigen tests

Enzyme Immunoassay based (EIA) or

Chemiluminescence based (CLIA) or

Immunochromatography (ICT)

- Monoclonal or Polyclonal anti *H.pylori* antibodies bind to antigens
  - ***Monoclonal superior accuracy***
  - ***AHMSG supports use of monoclonal SAT***

Non-invasive test Accuracy

Comparative accuracy of Non-invasive tests in a hypothetical cohort of 1000 patients with different prevalence levels

Prevalence (%)	Specificity	False positives	Test	Sensitivity (95% CI)	Missed cases (95%CI)
42.0	0.79	122/1000	UBT ^{13}C	0.98	10/1000
			SAT	0.92	32/1000
66.5	0.79	70/1000	UBT ^{13}C	0.98	16/1000
			SAT	0.92	51/1000
42.0	0.96	23/1000	UBT ^{13}C	0.86	57/1000
			SAT	0.65	146/1000
66.5	0.96	13/1000	UBT ^{13}C	0.86	90/1000
			SAT	0.65	231/1000

Best LMJ, et al. Non-invasive diagnostic tests for Helicobacter pylori infection. Vol. 2018, Cochrane Database of Systematic Reviews.

Performance of stool antigen-based diagnostic kits varies

Test	Gold standard method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Testmate Pylori antigen EIA (Wakamoto Pharmaceutical Co., Ltd., Tokyo, Japan)	Culture alone or histology and RUT combined	99.6	100			
Amplified IDEIA HpStAR (Thermo Fisher Scientific, Waltham, MA, USA)	Culture alone or histology and RUT combined	93.6	100	100	87.3	96
Diagnostec *H. pylori* antigen EIA kit (Reininghun Diagnostics Biomedical, Inc, Taiwan)	UBT	92.9	98.3	95.8	97.1	96.7
Diagnostec *H. pylori* antigen rapid test kit (Reininghun Diagnostics Biomedical, Inc, Taiwan)	UBT	92.9	95.8	90.1	97.0	94.9
H. pylori Quik Chek test (TechLab Inc., Blacksburg, VA, USA)	At least two of histology, culture, and RUT positive	91	100	98	97	
H. pylori Chek test (TechLab Inc., Blacksburg, VA, USA	At least two of histology, culture, and RUT positive	92	91	76	97	
Wondfo one-step *H. pylori* feces test	RUT	65.1	70.2	62.2	72.7	68

Variable accuracy depending on the antibody-antigen interaction and detection method

Non-invasive diagnostic tests for *Helicobacter pylori* infection (Review)

Cochrane Database of Systematic Reviews

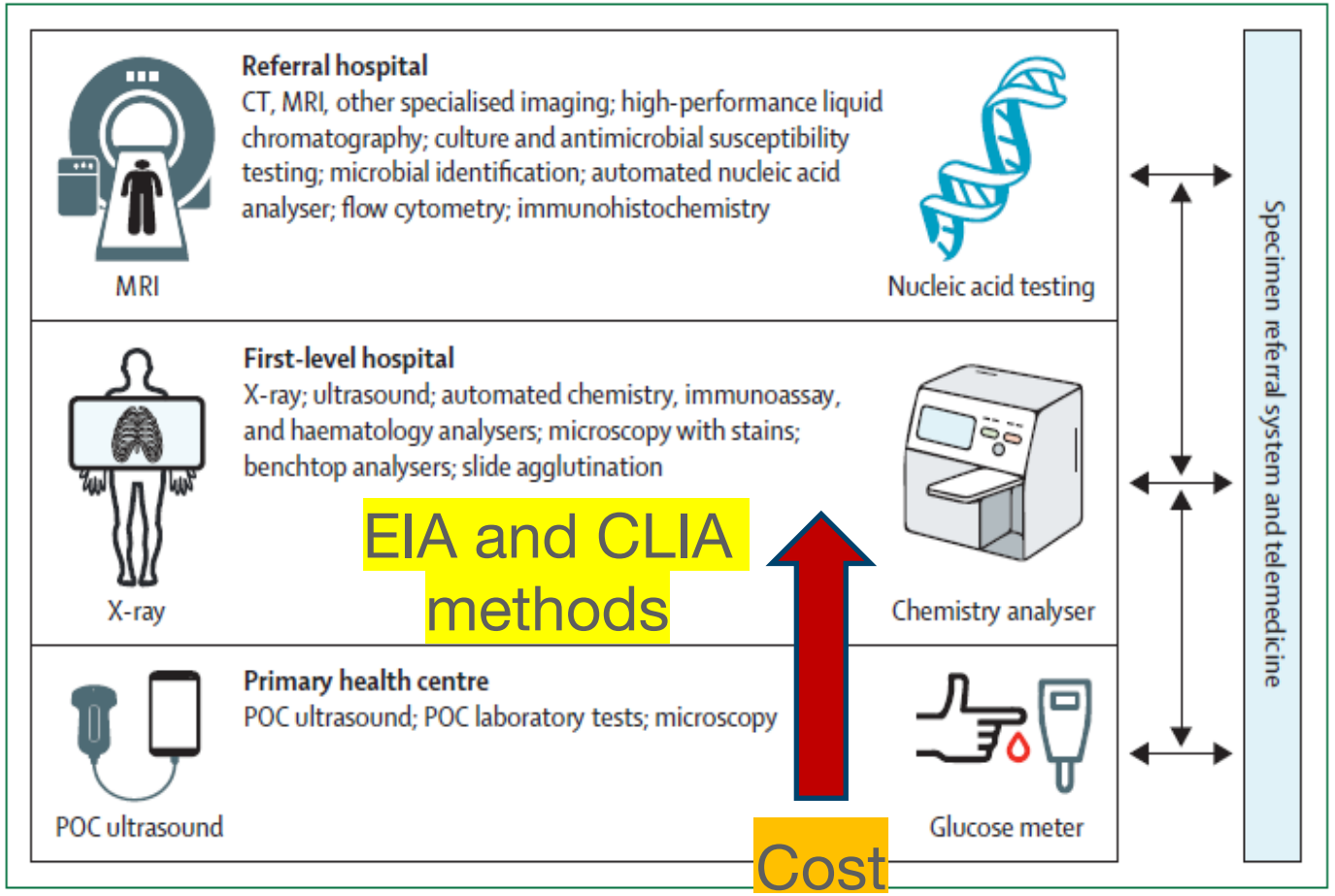
- 101 studies (11,003 participants); median *H.pylori* prevalence 53.7%
- Few direct comparisons between tests, but UBT 13C found to be the most accurate
- UBT 13C cumbersome , higher cost BUT more accurate
- SAT easy-to-use but with lower diagnostic accuracy

Best LMJ, et al. Non-invasive diagnostic tests for Helicobacter pylori infection. Vol. 2018, Cochrane Database of Systematic Reviews

Could SAT be used at Primary level?

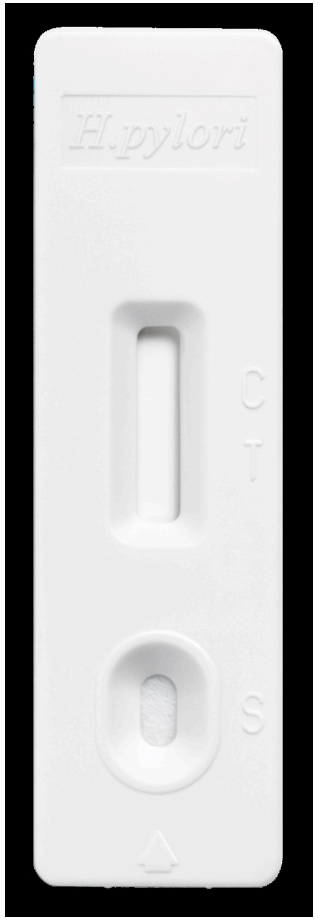
Primary health centre level testing

- Immediate result
- Convenience
- Decrease upstream costs such as logistics and processing

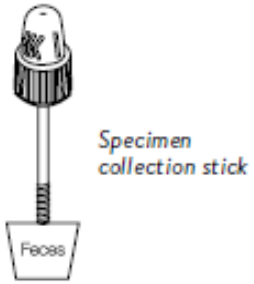


Rapid ICT

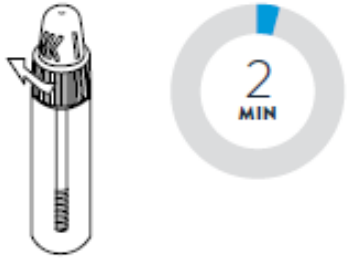
Antigens present in the stool samples migrate upward from the sample well and form an antigen-antibody complex at the test line



1 Collect the specimen

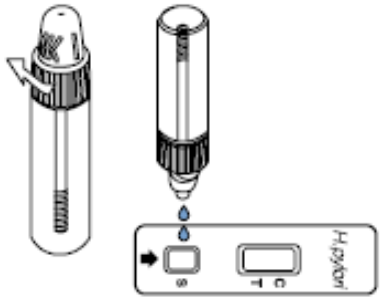


2 Screw on and tighten the cap of the specimen collection tube, leave the tube alone and wait 2 minutes



3 Unscrew and open the upper cap

2 drops (approx. 80 µL) of extracted specimen



4 Wait 10 minutes

Do not interpret the result after 20 minutes

Results interpretation

POSITIVE

NEGATIVE

INVALID

Clearview™ H.pylori Ag test Abbott

Diagnostic performance of fecal *Helicobacter pylori* antigen test in Uganda

Owot JC, et al. Diagnostic performance of fecal Helicobacter pylori antigen test in Uganda. BMC Gastroenterology. 2022 Dec

- **150 patients; rural Uganda with dyspepsia**
  - **Rapid ICT SAT (Clearview Abbott)** on faeces compared to PCR-16S rRNA *H.pylori* on gastric biopsy (used as the reference std)
  - Monoclonal anti-*H.pylori* antibodies
  - 59 positive for SAT
  - 67 positive PCR-16S rRNA
  - 57 positive for SAT and 16S rRNA

- **Sensitivity of 0.85 and specificity of 0.98**

ICT tests
- easy to perform
- do not require specialised equipment
- useful for developing countries

Shimoyama T. Stool antigen tests for the management of Helicobacter pylori infection. World Journal of Gastroenterology. 2013;19(45):8188–91.

Could UBT be used at Primary level?

- Traditional ^{13}C testing is expensive and requires skilled personnel
- Novel testing methods using infrared spectroscopy and laser assisted ratio analysis
  - Nondispersive isotope selective infrared spectroscopy (NDIRS)
- Decreased the cost and complexity of testing
- Possible home or POC test ?
- More study required…

First-time Urea Breath Tests Performed at Home by 36,629 Patients: A Study of *Helicobacter pylori* Prevalence in Primary Care

- 2003-2009
- 36,629 UBT performed using a home test approach
- UBT kit with a breath bag; capsule with 75mg 13C; instructional leaflet and a stamped envelope addressed to return to the lab
- 726/45,213 bags had errors

Other novel Primary health care level approaches…

New Rapid *Helicobacter Pylori* Blood Test Based on Dual Detection of FliD and CagA Antibodies for On-Site Testing

- New *H.pylori* POCT for whole blood, serum or plasma, based on the detection of 2 highly specific and sensitive antibodies flagellar filament capping protein (FliD) and cytotoxin-associated gene A (CagA)

Key highlights and takeaways

- **A ‘test and treat’ strategy for SSA is recommended by AHMSG**
- SSA has a high prevalence of *H.pylori* but a low incidence of GC
    - ? Population life expectancy shorter / ?Poor access to healthcare resources / ?Poor documentation
    - Could we see the incidence of GC change
- SAT is the preferred non-invasive test due to the limited access to UBT
- **SAT can be performed in the Primary health centre using rapid ICT with high sensitivity and specificity such as Clearview *H.pylori* test**