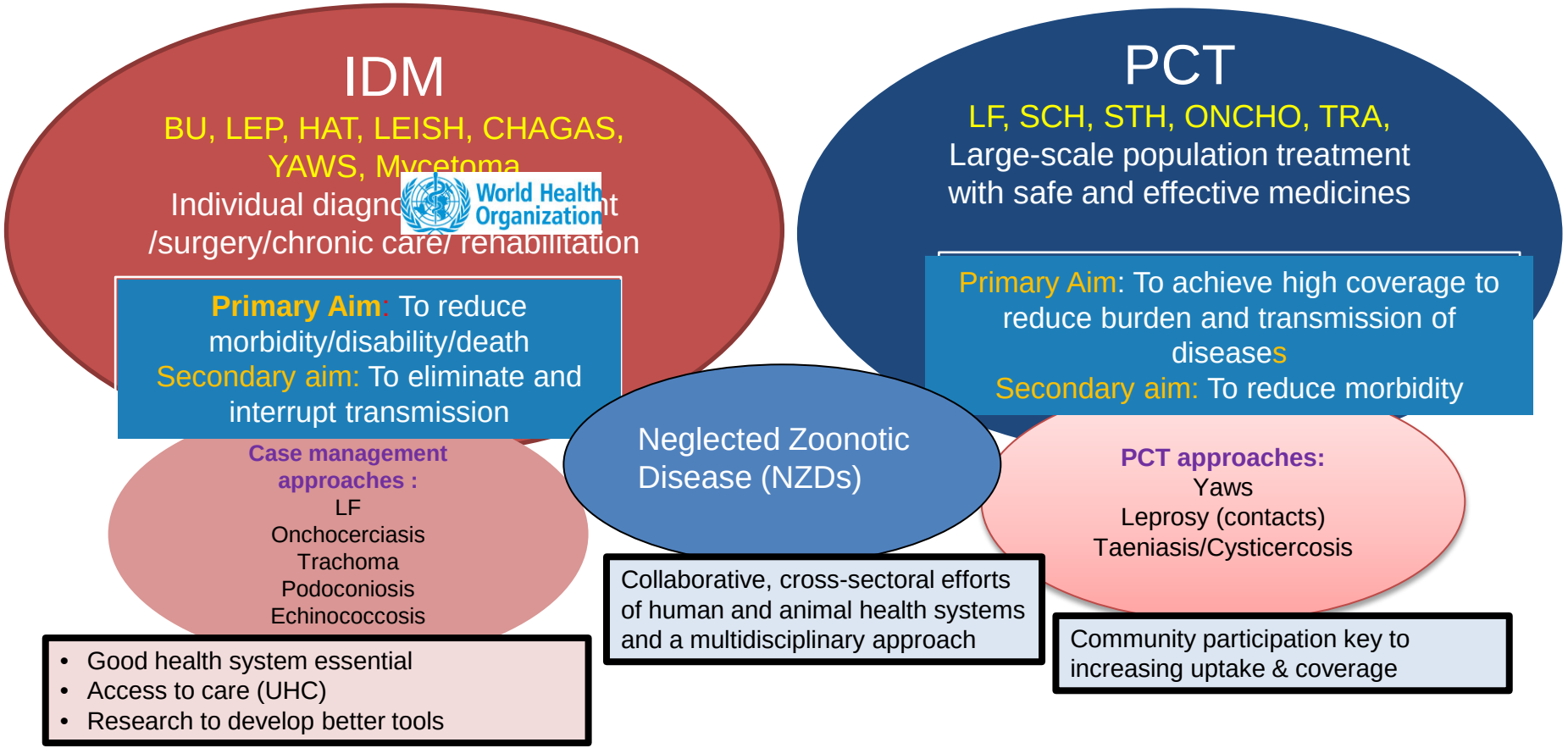
Overview of IDM (Case management) NTDs Laboratory Diagnosis and Diagnostic needs

Dr Daniel Argaw Dagne

IDM/NTDS, WHO

World Health Organization

Neglected Tropical Diseases



Some features of CM NTDs

- Disease are prevalent in the remotest areas- marginalized communities – weak health services
- Focal distribution and clustering around the same communities
- Several vectors and reservoirs involved
- Diverse diseases groups – could be fatal if not treated or may lead to deformity, disfiguring, disability
- Stigma and discrimination
- Case management – diagnosis may involve multiple steps, clinical staging or severity assessments, use of potentially toxic drugs or drugs with many side effects

IDM/NTDs strategy – Building on Successes & lessons learnt from Individual disease control, elimination or eradication programmes

IDM NTDs –UHC, SDG agenda:

100% of the population with access to affordable diagnosis, treatment and care for NTDs, leading to 100% of the population at risk protected against out-of-pocket payments due to NTDs by 2030.

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Diagnostics are essential in all phases of IDM NTDs control

Case detection/diagnosis is the centrepiece in the IDM/NTDs control, elimination or eradication strategy

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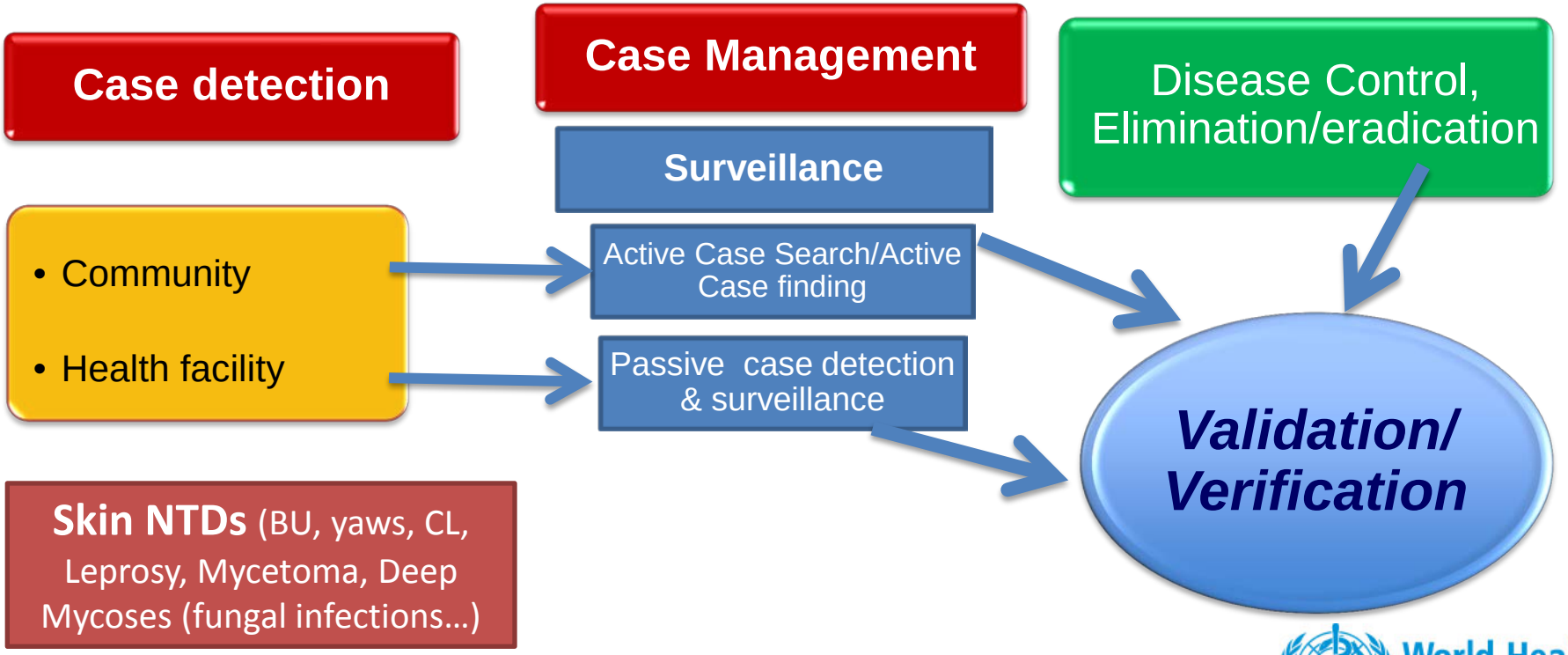
Diagnostics are essential in all phases of IDM NTDs control



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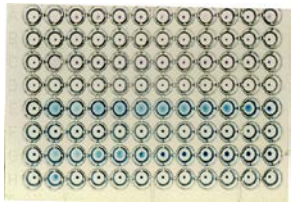
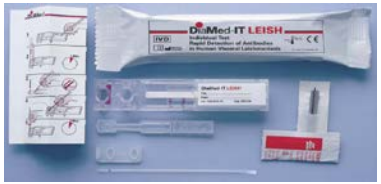
CM NTDs Diagnostics - current





- Current diagnostic methods for case management (IDM) diseases are not satisfactory
- Diagnosis is based on demonstration of the parasites in tissue aspirates or blood, detection of antibody to the parasites, detection of parasite products in the blood or body secretions, or quantitative/qualitative detection of parasite DNA.
- Most of the diagnostic tests require invasive sampling and lack appropriate sensitivity and specificity.
- Multiple steps or extended algorithmic and/or combination of tests to reach diagnosis

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Table 4

Summary of characteristics of available diagnostics

Disease	Parasite demonstration			Parasite DNA detection			Serology		
	Source	Sensitivity	Specificity	Test	Sensitivity	Specificity	Test	Sensitivity	Specificity
Chagas disease	Blood	>70% when smear performed 15–30 days after onset of symptoms (only in the acute phase)	100%	PCR RT-PCR	~60% (in children)	If properly done, can be 100%	IHA , IIF, ELISA (chronic phase)	94%–99.5% (kit-dependent difference)	94%–96% (kit-dependent difference)
Human African trypanosomiasis	Blood	44.8%–91% (combination including mAECT)	~100%	PCR RT PCR LAMP	~95%	~100%	CATT	68%–99.5% (regional differences)	83.5%–98.4%
Visceral leishmaniasis	Spleen	90%–95%(smear)	~100%	PCR RT-PCR	~95%	~100%			
	Bone marrow	60%–85%(smear)	~100%	PCR RT-PCR	~95%	~100%			
	Lymph node	50%–60%(smear)	~100%	Not extensively studied					
	Blood			PCR RT-PCR	~80%–95%	~100%	DAT ELISA rK39-ICT	91%–100% 85%–95% 90%–100%	72%–100% 70%–85% 93%–100%
Cutaneous leishmaniasis	Skin	30%–90% depending on the parasite species (smear)	~100%	PCR	~90%–95%	~100%			
	Lymph node	40%–70% in *L. braziliensis* infections (aspirate culture)	~100%	Not extensively studied					

CATT, card agglutination test for trypanosomiasis; DAT, direct agglutination test; ELISA, enzyme-linked immunosorbent assay; ICT, immunochromatography test; IHA, indirect haemaglutination; IIF, indirect immunofluorescence; LAMP, loop mediated isothermal amplification; mAECT, miniature anion exchange centrifugation technique; PCR, polymerase chain reaction; RT-PCR, reverse transcriptase polymerase chain reaction.

Current & potential roles of diagnostics for IDM NTDs

Roles	General Test performance requirements
Case detection/screening diagnosis	High sensitivity
Individual case diagnosis and management	High sensitivity and specificity – case confirmation is required for case management
Prevalence & epidemiological surveys - High prevalence - Low prevalence	 - Medium sensitivity - High sensitivity
Verification of elimination; Post-elimination surveillance	- High throughput tests – as large no. of people, vectors or intermediate hosts may need to be sampled; high sensitivity and specificity
Differentiate new infections vs relapses/past	High specificity, point-of-care test
Other roles: drug resistance monitoring; test of cure, clinical prognosis, progression from infection to disease …	

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Currently used diagnostic methodologies

CM (IDM)NTDs	Diagnosis	Tests used	Remarks
Buruli Ulcer	Clinical; PCR; Microscopy; histopathology & culture	Microscopy – ZN AFB; PCR; TLC	PCR most commonly used methods
Chagas Disease	Parasitology; Serology Epid link; xenodiagnosis, imaging	RDTs; Indirect Haemaglutination, Indirect immunoflourescence, ELISA	Microscopy in the acute phase of infection
Human African trypanosomiasis	Clinical + Epid link & Serology & parasitology	CATT; RDTs; TL; PCR; mAECT; LAMP; microscopy	Multiple steps – screening, parasitological, staging
Leishmaniasis (Cutaneous & MCL)	Clinical + Epid link &/or Microscopy; culture	Microscopy-Giemsa stain; PCR; LST	Commonly clinical & skin smear
Leishmaniasis (VL)	Clinical + Serology or Parasitology; PCR	RDTs (rk39, rk16, rk 28); PCR; DAT; IFAT; ELISA ..	RDTs commonly used methods- perform well in certain regions
Leprosy	Clinical signs; slit-skin smears or nerve biopsy	Slit-skin smear –ZN stain-AFB	3 cardinal signs
Mycetoma; deep mycoses (Fungal Skin infections)	Clinical + Epid &/or Microscopy or histopathology; culture, imaging	Cytological, histochemical, microscopy, X-ray, US, CT, MRI	Invasive, time consuming, combination of tests
yaws	Dark field Microscopy; Serology, PCR	TPHA/TPPAA; RPR &VDRL; Multiplex Assay, DPP, PCR	One confirmed case is required for MDA

Case management NTDs – diagnostic needs

CM (IDM)NTDs	Diagnostic needs not in the order of priority
Buruli Ulcer	RDTs – POC; screening tests; monitoring drug effectiveness
Chagas Disease	POC for acute infection, chronic Chagas, congenital Chagas, assessment of treatment, cure vs relapse; prognostic tests (Biomarkers predictive of disease progression
Human African trypanosomiasis	Non-invasive POC RDT to detect & Staging; test of cure; surveillance of drug resistance; verification elimination; post-elimination surveillance
Leishmaniasis (Cutaneous & MCL)	POC RDT for CL -confirmatory, Mucocutaneous leishmaniasis; DCL
Leishmaniasis (VL)	Improved RDTs, prognostic tests, TOC, prognostic test, monitoring drug resistance; optimized test for VL in HIV coinfection, diagnosis of PKDL
Leprosy	Diagnostic-early diagnosis/Confirmatory tests; monitoring treatment & resistance
Mycetoma; deep mycoses (Fungal Skin infections)	Simple POC RDTs, monitoring treatment/ drug efficacy
yaws	Diagnostics to guide when to stop MDA; post-elimination surveillance

Summary – IDM Diagnostic Gaps & Needs

- Point-of-care (POC) RDT – new or improved POC diagnostics for case detection and diagnosis and epidemiological surveillance
- Test of cure and diagnostics for clinical trials –end- point
- Diagnostics for drug resistance monitoring
- Verification of elimination, post-elimination surveillance
- Simplification, standardization and field-friendly modifications are needed for meaningful application of PCR
- Exploring digitization – new platforms, possible synergies for integrating of testing approaches
- As the sensitivity and specificity of a method may vary in different endemic regions, the selection of the diagnostic tests should be based on several parameters, including the sensitivity and specificity as well as the cost, the availability of equipment and qualified personnel, rapidity and field applicability.
- Ensuring utilization of available diagnostics - access

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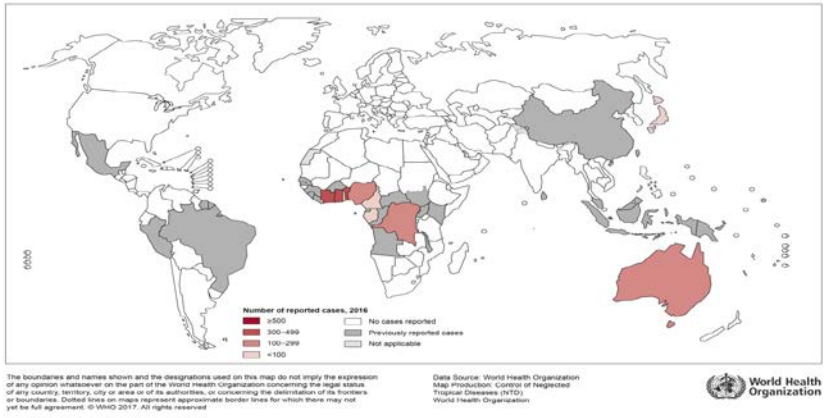
Buruli ulcer control

- WHO's recommendation to use a combination of antibiotics treatment in 2004 marked a major advance in Buruli ulcer control

- The comparative study with Rifampicin & streptomycin versus rifampicin & clarithromycin (oral) completed and oral antibiotic therapy recommended for control and treatment

Distribution of Buruli ulcer, worldwide, 2016



Buruli ulcer cases reported 2002-2016

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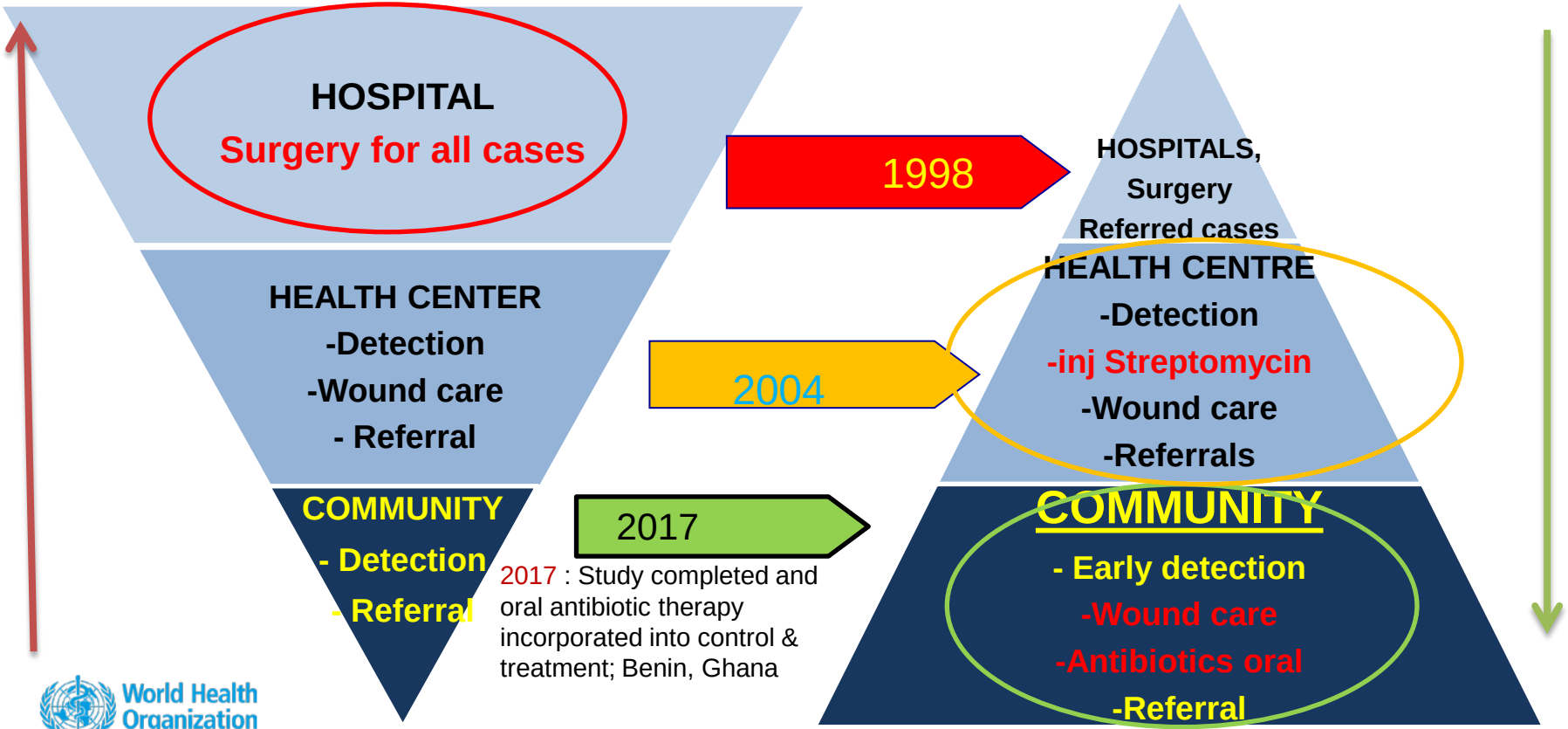
Before antibiotics

After antibiotics



2017 : Study completed and oral antibiotic therapy incorporated into control & treatment; Benin, Ghana

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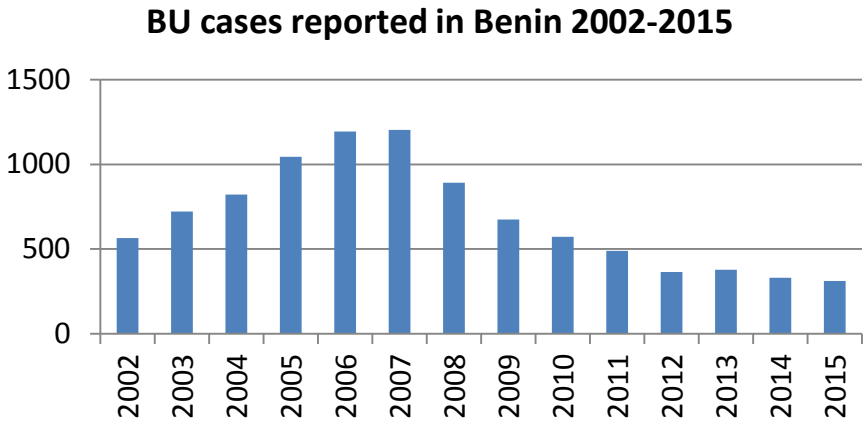
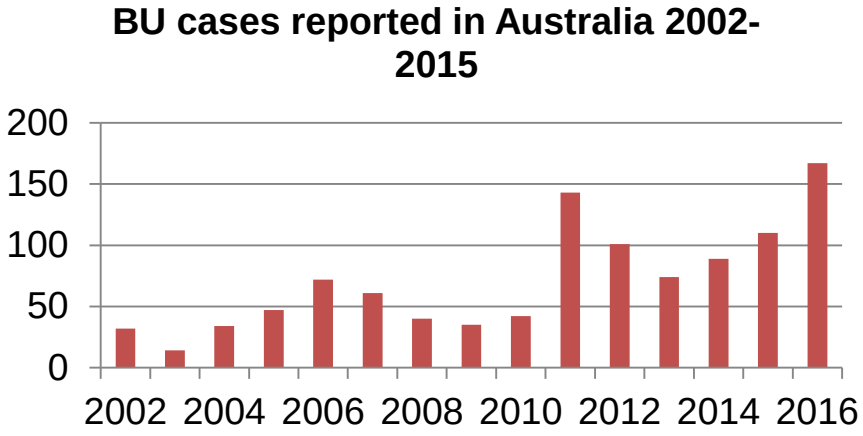
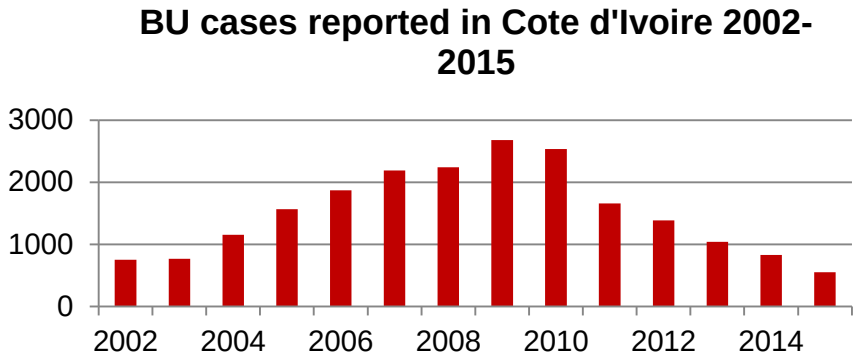
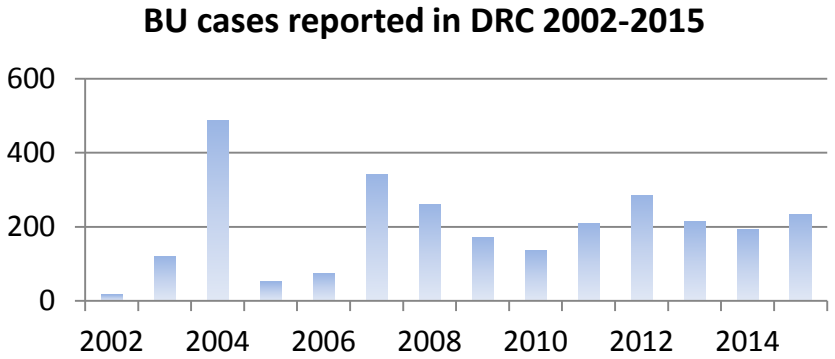
Epidemiology – Selected countries



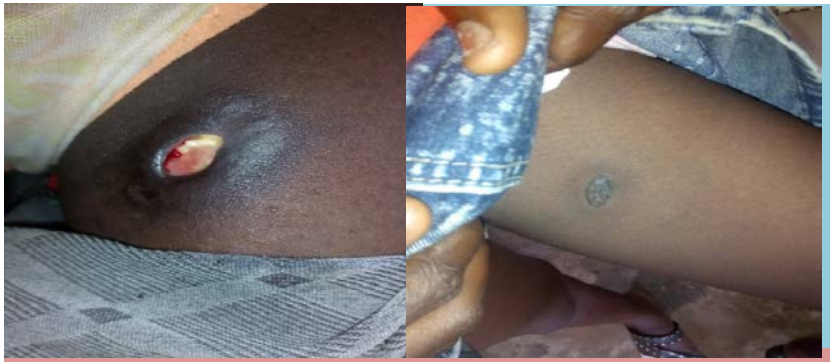






Buruli ulcer

Research progress and priorities



Antibiotic treatment (oral)

Development of diagnostic test

Mode of transmission

Antwerpen
16-20 October 2017

Figure 1. Key axes of Buruli ulcer strategy

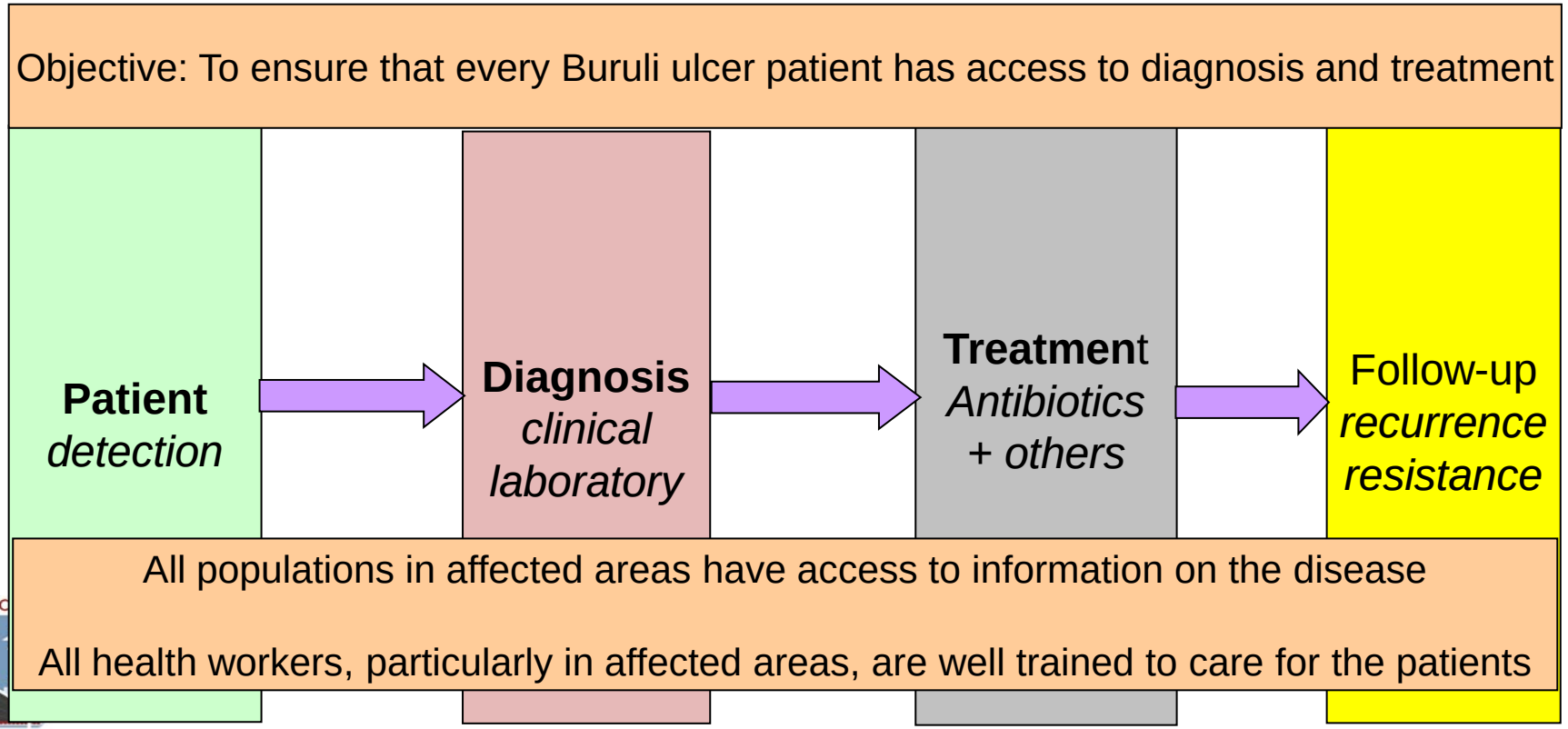
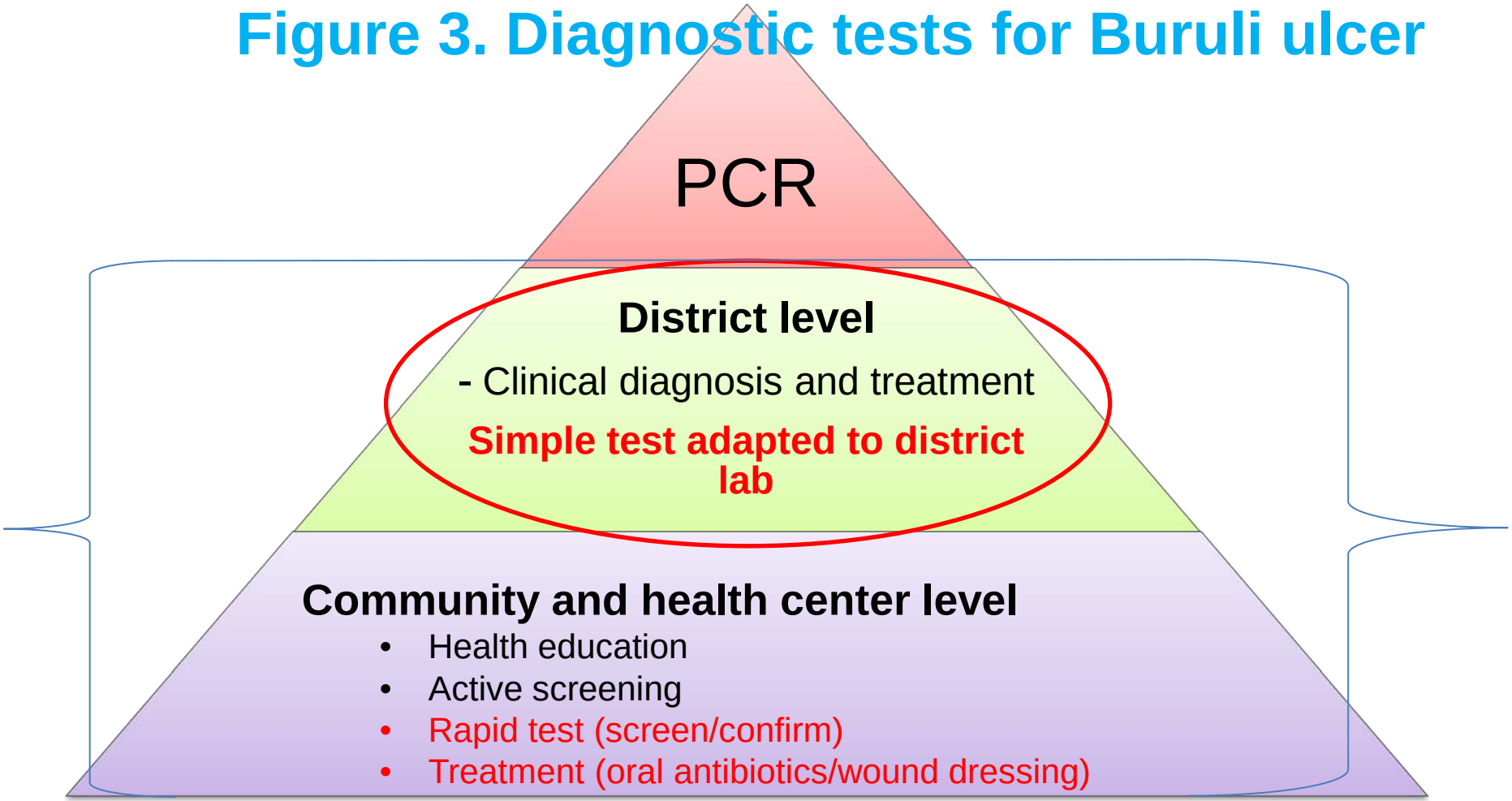


Figure 3. Diagnostic tests for Buruli ulcer



Research priority 1:

Simplification antibiotics treatment

Current Treatment

Rifampicin &
Streptomycin for 8 weeks
but strept is by injection – pain,
Toxicity, contraindication
in pregnancy

Ultimate goal

Complete oral therapy

Study completed 2017
(manuscript in progress)

Research priority 2:

Diagnosis and development of tests

Clinical diagnosis is possible but difficult for non-ulcerative disease

PCR is sensitive >98% but not available in remote rural clinics

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Mycolactone detection test

Antigen capture and human biomarkers but in discovery phase

Simplified PCR

Thank you

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