

Joint annual meeting
Swiss Society for Infectious Diseases (SSID)
Swiss Society for Hospital Hygiene (SSHH) / fibs / SIPI
Swiss Society of Tropical and Travel Medicine (SSTTM)

September 13 – 15, 2023

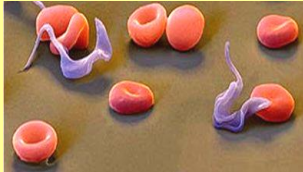
Human African trypanosomiasis (sleeping sickness)

Update & outlook

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Human African trypanosomiasis (HAT, sleeping sickness)



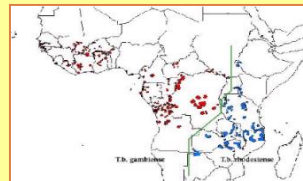
Agent: Trypanosome

T. b. gambiense

T. b. rhodesiense



Vector: Tsetse fly (*Glossina*)



Focal distribution, sub-Saharan Africa



Affects neglected populations



Lethal without treatment

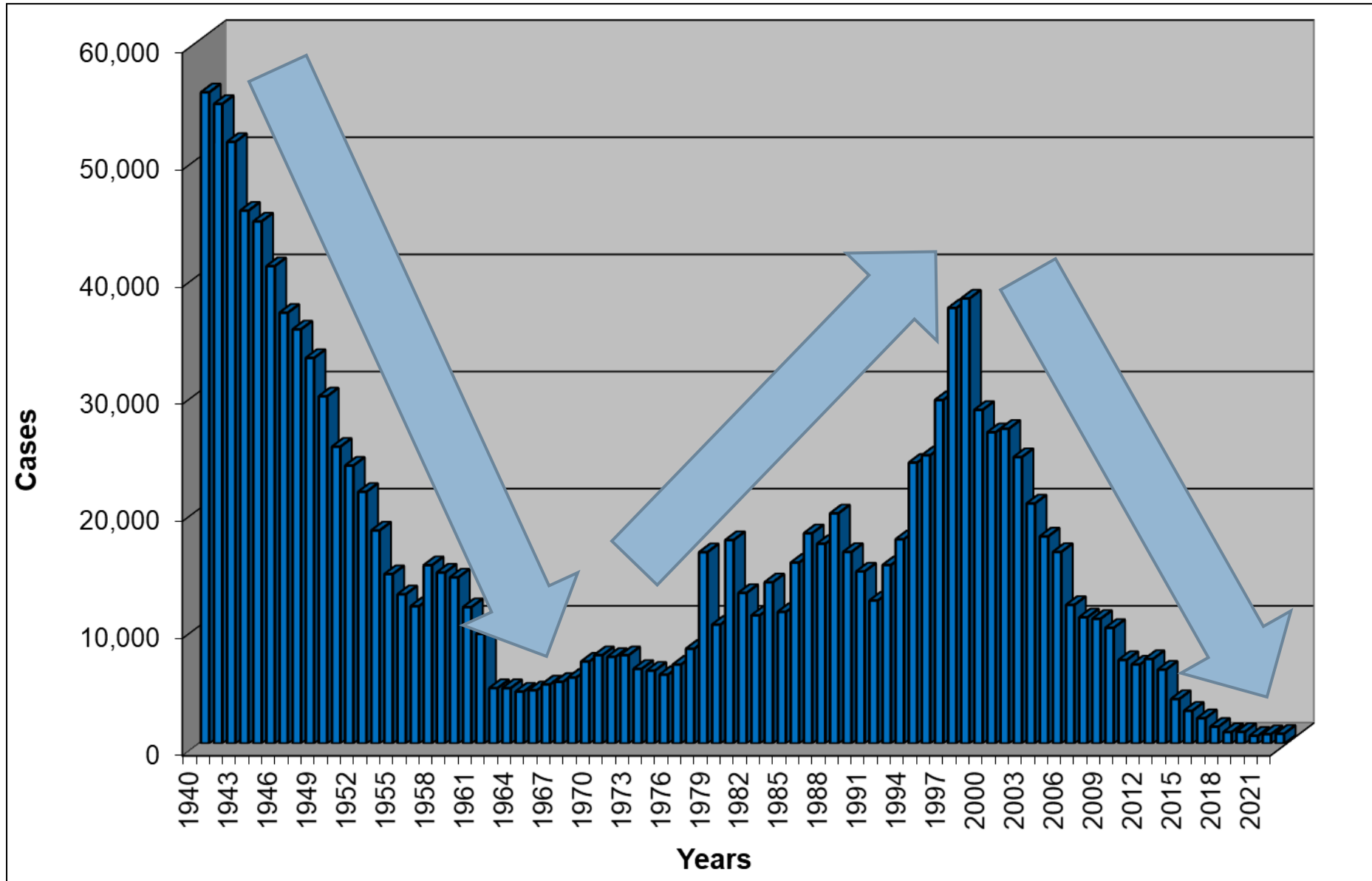
HAT distribution



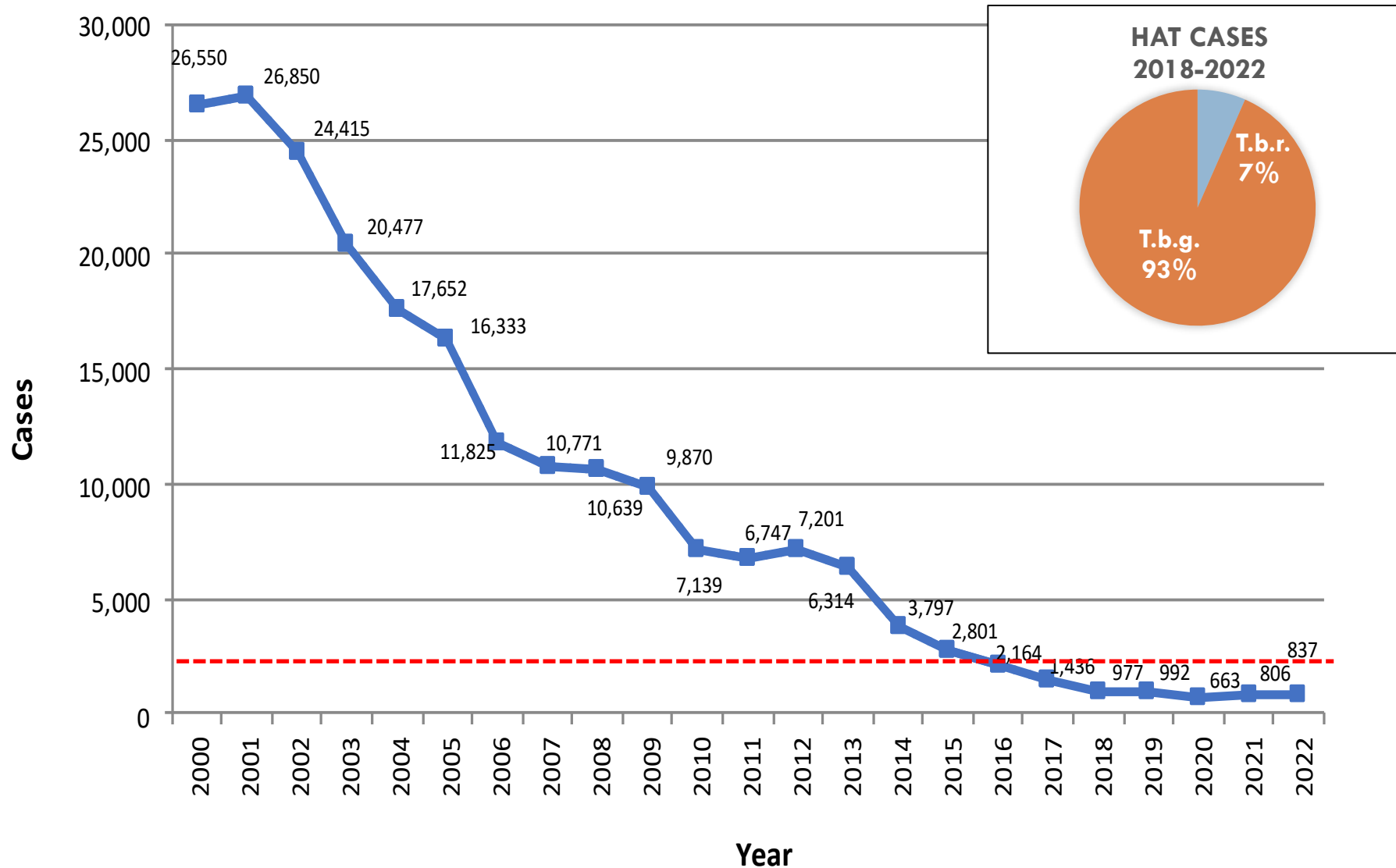
36 endemic countries

- ***T. b. gambiense***: Angola, Benin, Burkina Faso, Cameroon, Chad, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Gabon, The Gambia, Ghana, Guinea, Guinea Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leona, South Sudan, Togo, Uganda
- ***T. b. rhodesiense***: Botswana, Burundi, Eswatini, Ethiopia, Kenya, Malawi, Mozambique, Namibia, Rwanda, Uganda, United Republic of Tanzania, Zambia, Zimbabwe

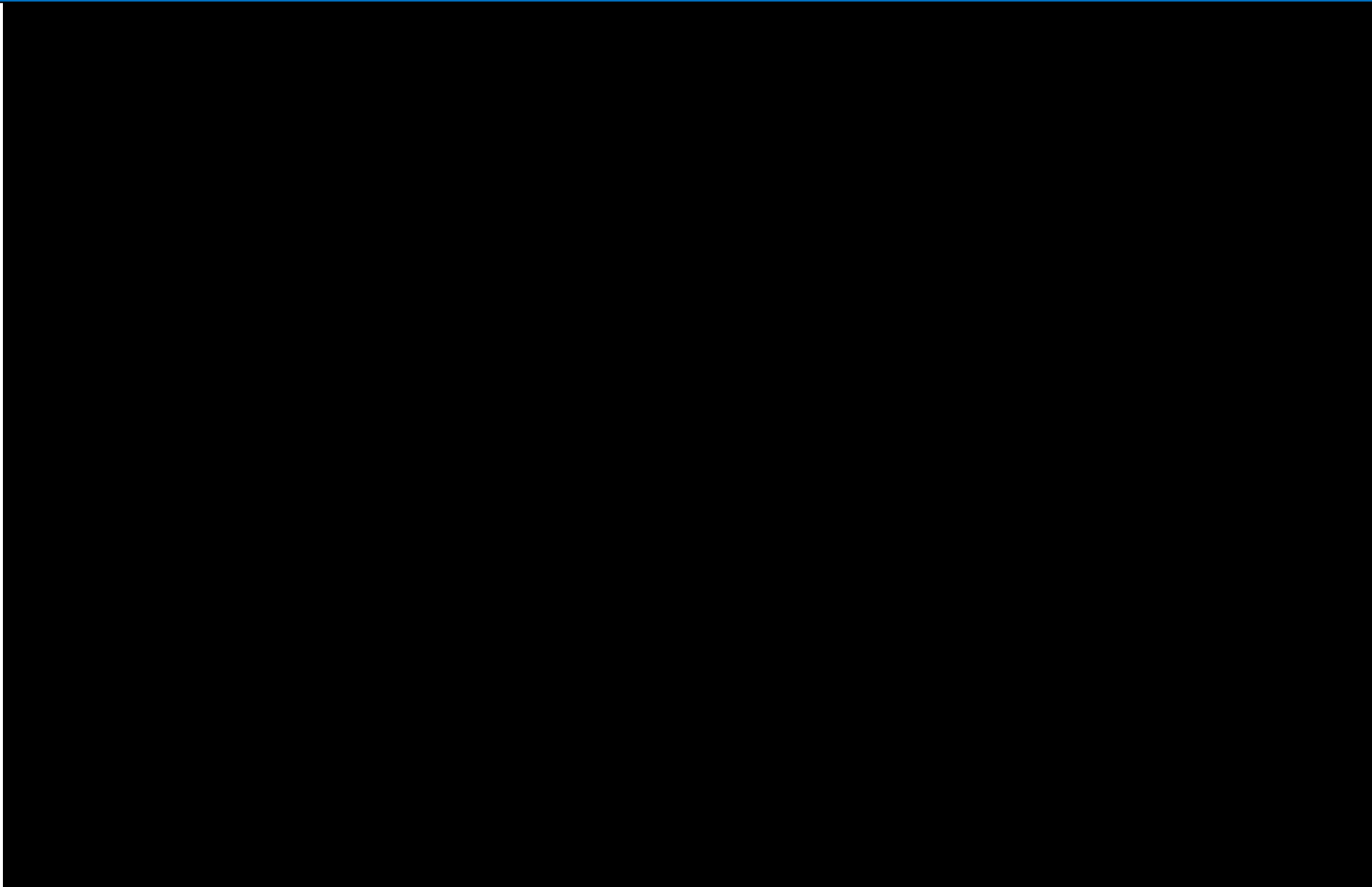
Cases HAT reported. 1940 – 2022.



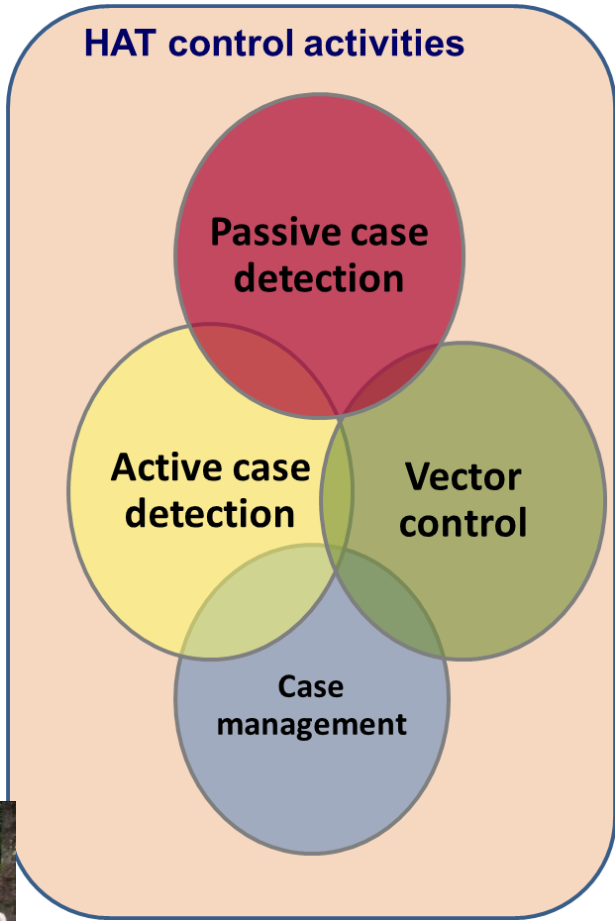
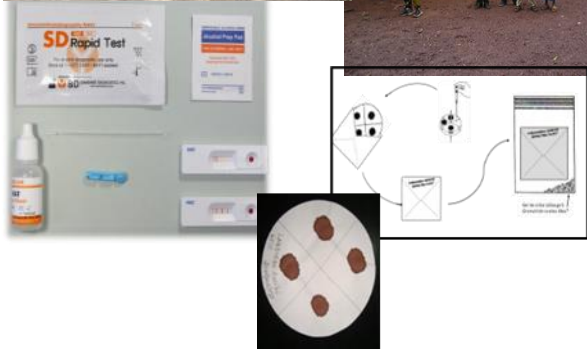
HAT: New cases reported, 2000-2022.



HAT: Areas at risk, 2000-202.



HAT: WHO control & surveillance Strategy



Human African trypanosomiasis: Diagnosis

HAT can hide

- HAT signs and symptoms: unspecific
- Cases may pass for other diseases
- The diagnosis of HAT depends on the laboratory
- Suspicion depends on awareness

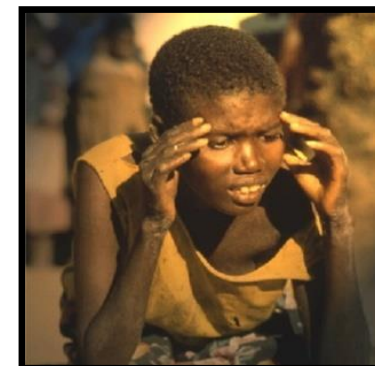


HAT: Clinical Suspicion (epidemiological context)

Epidemiological antecedents

Clinical Symptoms and signs

- **Cutaneous:** Chancre, pruritus, rash (trypanides), oedema (“moon facies”)
- **Enlarged lymph nodes:** subclavicular & cervical (“Winterbottom sign”)
- **Fever:** irregular, accompanied by headaches, fatigue, myalgias, arthralgias, anorexia
- **Hepatomegaly & splenomegaly**
- **Endocrine dysfunction:** Amenorrhea, thyroid dysfunction, adrenal insufficiency and hypogonadism
- **Neuropsychiatric:** Sleep disorders, tremor, motor disturbance, hyperesthesia, ataxia, abnormal gait, abnormal movements (choreoathetosis), speech disorders, psychiatric disorders (aggressivity, antisocial behavior, apathy, confusion, delirium, convulsions...)
- **Cardiopathy:** perimyocarditis, ECG alterations
- **Renal failure**
- **Biochemical signs:** Reduced hematocrit, Increased VSG, Increased IgM and IgG, leukocytosis, thrombocytopenia



HAT: Serological suspicion

In the field:

- **Card agglutination test for trypanosomiasis (CATT)**

Sensitivity: 78.1-99.8%

Specificity: 93.4-99.2%

RDT

- **SD Bioline HAT 2 (SD/Abbott[©])**

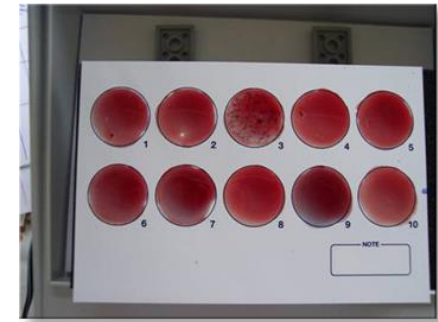
Sensitivity: 71.2-96.8%

Specificity: 79.0-98.1%

- **HAT Sero-K-Set (Coris/Avacta[©])**

Sensitivity: 98.5-100%

Specificity: 79.7-98.6%



Only for gambiense HAT

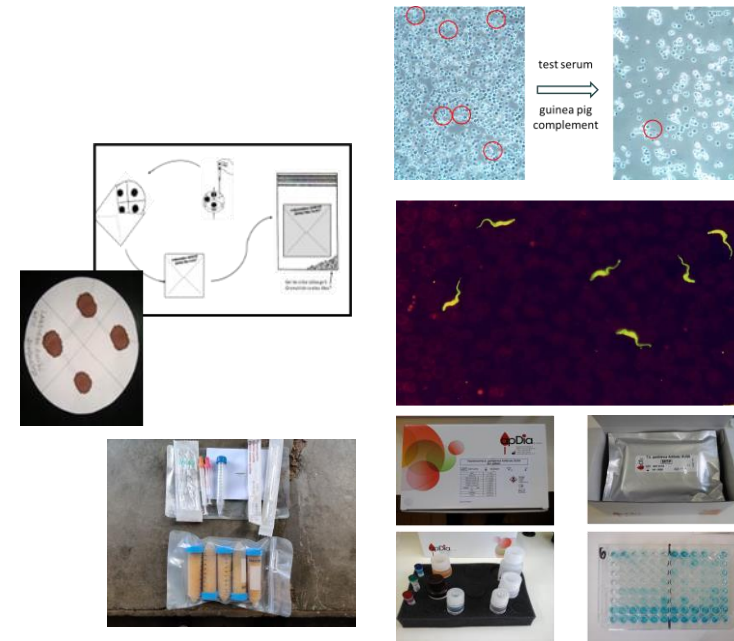
Availability not ensured

Limited specificity and sensitivity, variable according to settings

HAT: Strong serological suspicion

In the reference lab:

- **ImmunoTrypanolysis** (*T. b. gambiense*).
- **Immunofluorescence (IFAT)** (*T. b. gambiense* + *T. b. rhodesiense*)
- **ELISA** (*T. b. gambiense* + *T. b. rhodesiense*)

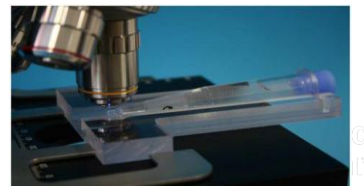
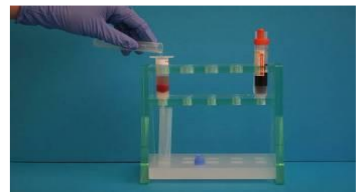
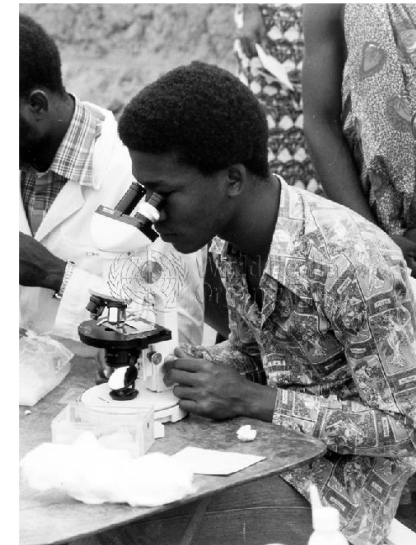
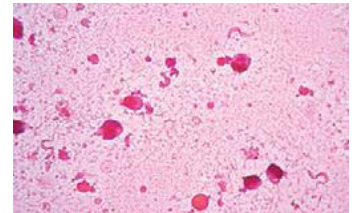


	throughput	antigen N / R	laboratory level	technical skill	DBS
Trypanolysis	low	N/R	high	high	yes
Immunofluorescence	medium	N	low	medium	yes
Indirect ELISA	high	N/R	medium	medium	yes
Inhibition ELISA	high	N/R	medium	medium	yes

HAT: Parasitological confirmation

Microscopy: Confirmation of diagnosis by detecting the parasite in body fluids

- Have limited sensitivity (60-90%), require specific skills and resource and time-consuming
 - **Lymph aspirate examination**
 - **Chancre exudate examination**
 - In blood
 - **Fresh bold examination**
 - **Thick/thin blood film**
 - **Micro-heamatocrit examination (CTC)**
 - **Quantitative buffy coat (QBC)**
 - **Mini-anion exchange centrifugation (mAECT)**
 - **Skin and other tissues??**
 - **CSF centrifugate**



Microscopy is less and less used

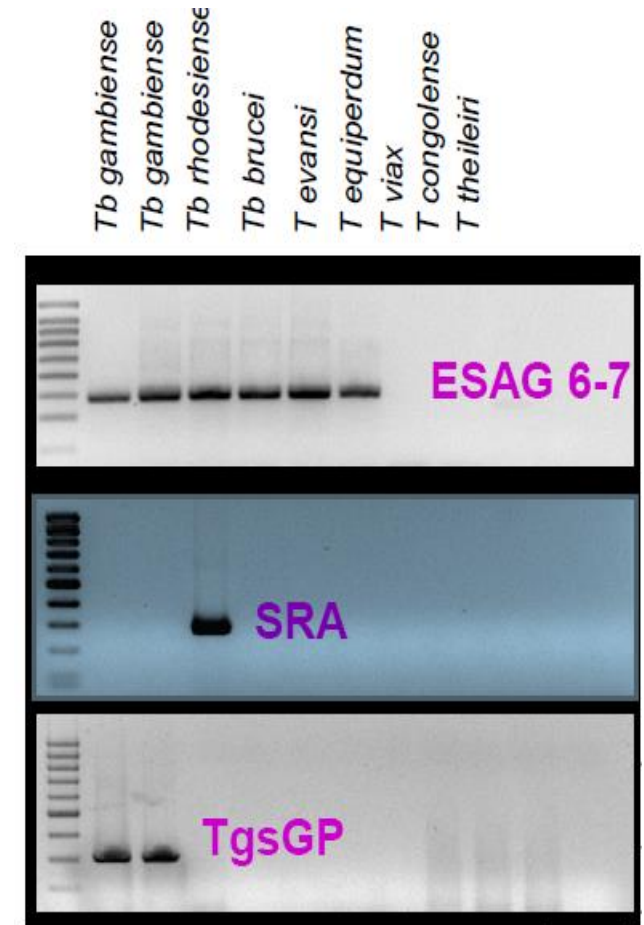
HAT: Molecular biology (direct evidence)

Molecular diagnosis: A surrogate for microscopic parasite detection

- Subject of numerous investigations but should be interpreted with caution in clinical practice.
- Sensitivity and specificity variable depending on:
 - Sampling: blood serum, buffy coat, CSF, skin and tissues, lymph
 - Transport: DBS, frozen samples, buffers
 - Targets (DNA, RNA): multicopy or single-copy
 - **Trypanozoon-specific PCR assays** (ESAG 6-7, TBR, 18S-DNA, 18S-RNA, SL-RNA,...)
 - **Subspecies specific**
 - T. b. gambiense-specific (**TgsGP**, kDNA, SNPs)
 - T. b. rhodesiense-specific (**SRA**)
 - Amplification: isothermal or PCR, SHERLOCK
 - Detection: colorimetric, fluorescence, lateral flow

Currently “home made” (poor reproducibility).

Limited diagnostic accuracy (limited specificity or sensitivity).



HAT: Treatment

First-line treatment for HAT (until 2019)

Gambiense-HAT

Adults and children

1 st stage	Pentamidine (1940)
2 nd stage	NECT (nifurtimox-eflornithine combination) (2009)

Rhodesiense-HAT

1 st stage	Suramin (1922)
2 nd stage	Melarsoprol (1949)

HAT: Treatment

First-line treatment for HAT (since 2019)

Gambiense-HAT

Adults and children ≥ 6 yrs

Children < 6 yrs

1 st stage	Fexinidazole (2021) (oral)	Pentamidine
2 nd stage <100 WBC/ μ L CSF		NECT
2 nd stage ≥ 100 WBC/ μ L CSF	NECT (2009)	

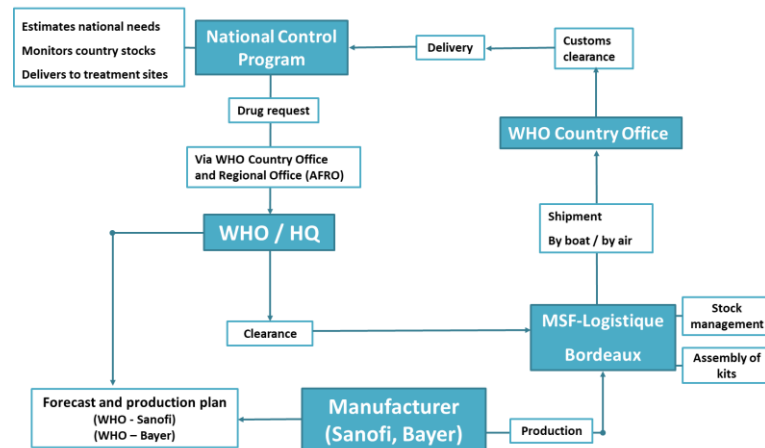
Rhodesiense-HAT

1 st stage	Suramin (1922)
2 nd stage	Melarsoprol (1949)

HAT: Treatment

- All the medicines are donated by the manufacturers (Sanofi and Bayer), and WHO ensures their worldwide distribution free of charge.

Drug supply system for Human African Trypanosomiasis



In non-endemic countries,

- Request directly to WHO. Small stocks placed in strategic centers
- Use of nifurtimox in HAT is off label
- Fexinidazole is not approved for its use out of endemic countries

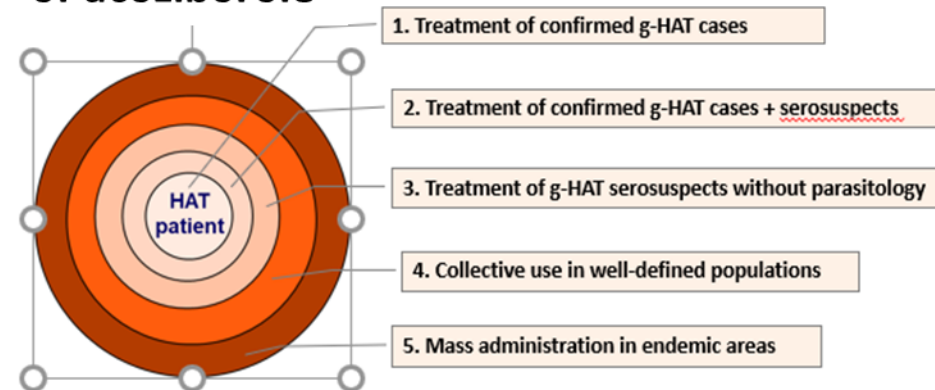
HAT: Treatment. Perspectives

Acoziborole

- Single oral dose
- Effective in gHAT first and second stage (208 patients treated, 95% of efficacy)
- Safety ?
- Effective in rHAT??
- Still not available and not approved



Expanded use of acoziborole

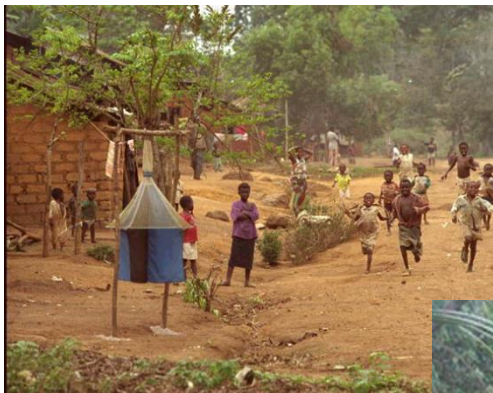


Fexinidazole (™)

- For rHAT, both stage: Under study

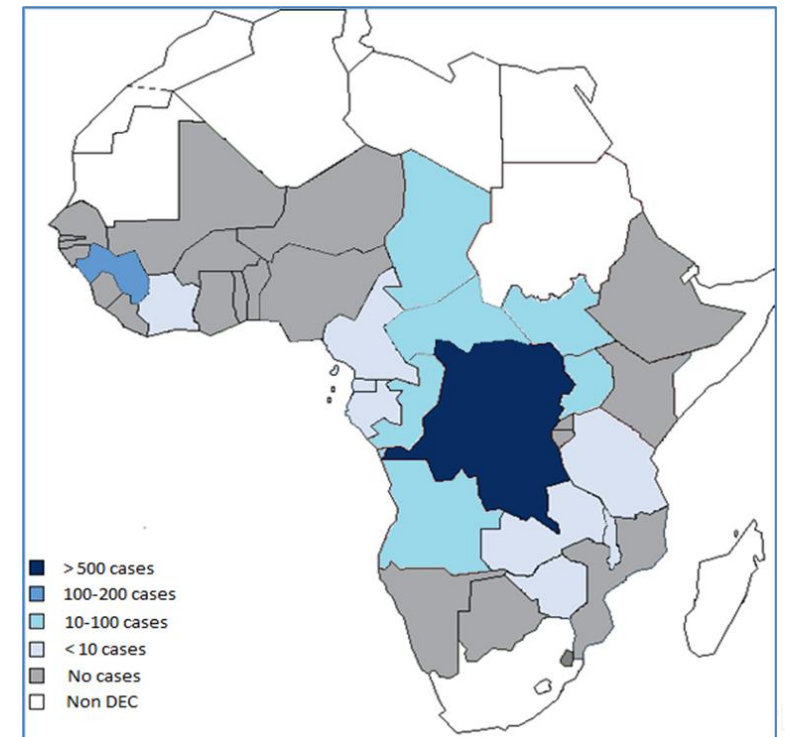
HAT: Vector control

- To be targeted in selected sites according to medical results
- Vector control methods have to be chosen according to local conditions (species, local resources, environment,...)
 - Traps and impregnated screens
 - Aerial or terrestrial spraying of insecticides
 - Selective spraying of animals
 - Release of sterile males



HAT: Control and surveillance. Current situation

- Thanks to sustained and coordinated efforts over the past 15 years, the number of reported cases has fallen to an historically low level. Fewer than 1000 cases were reported in 2019. Today, the disease has become rare.
- This important progress in the HAT control has allowed to target the disease for elimination by WHO.
- However, cases are reported from more than 20 countries in Africa.
- In the absence of a vaccine, disease control relies on case detection and treatment, and vector control.



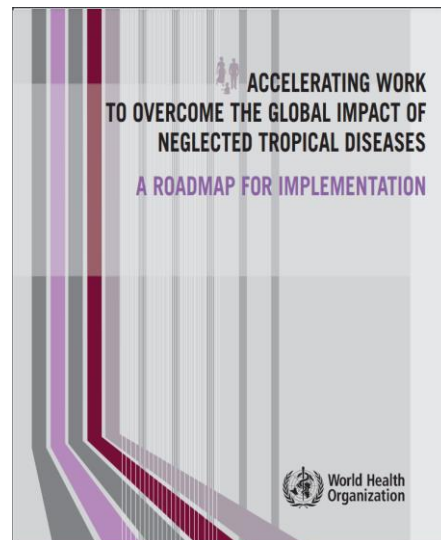
HAT elimination

THE WHO ROADMAP FOR NTDs 2021-2030

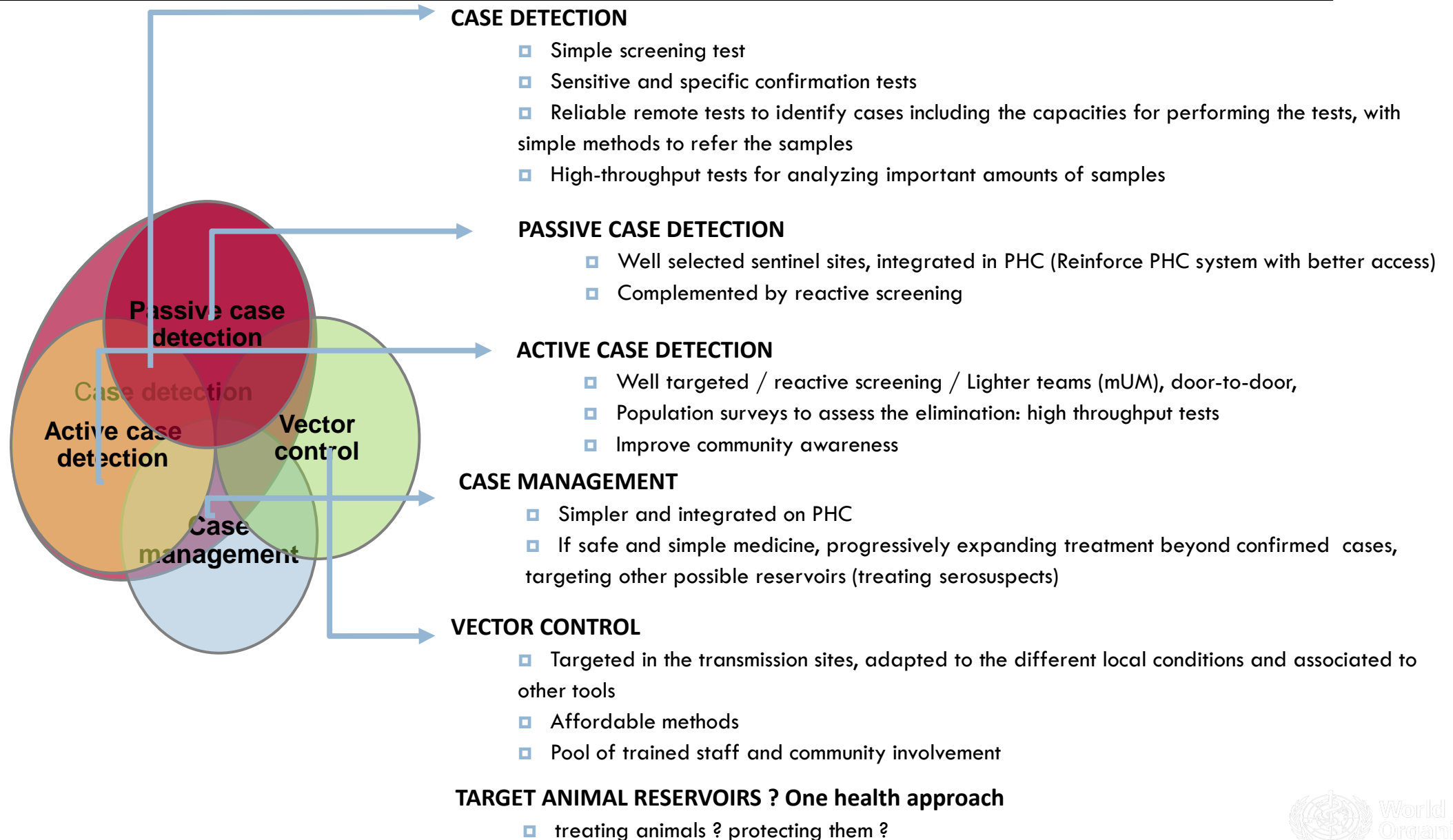
Goal 2030: "To interrupt transmission of gambiense HAT (sustainable elimination) by 2030 (zero case)"

WHO 2030 target, sub-targets and milestones

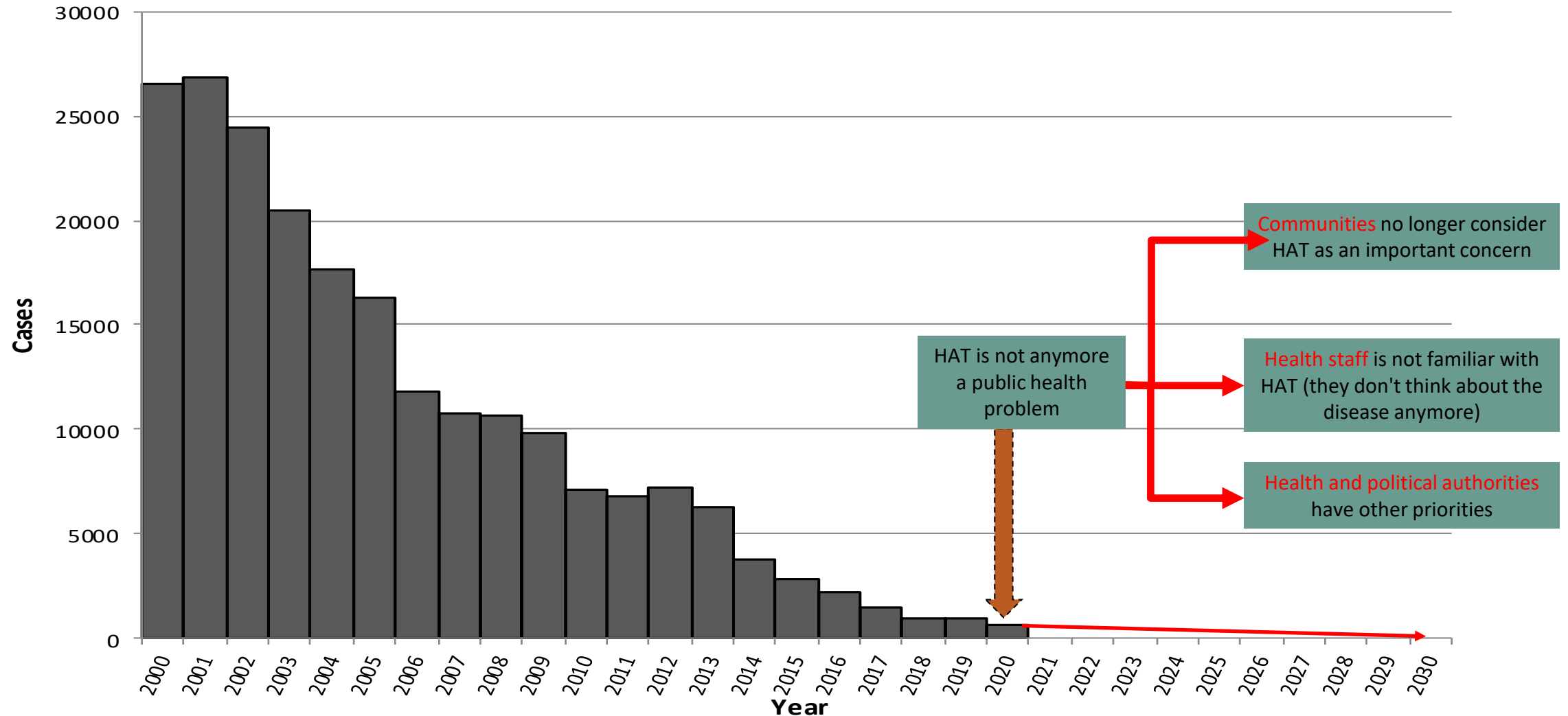
Indicator	2020 (provisional estimate)	2023	2025	2030
Number of countries verified for interruption of transmission	0	0	5 (21%)	15 (62%)
Number of gHAT cases reported	<1000	500	200	0



Strategies for HAT elimination



HAT elimination 2030: Challenges



HAT: cases in non-endemic countries

- Cases are also diagnosed outside endemic African countries among travelers, tourists, expatriates, and migrants.
- Human African trypanosomiasis should be considered in differential diagnosis for individuals who have visited or lived in endemic areas.

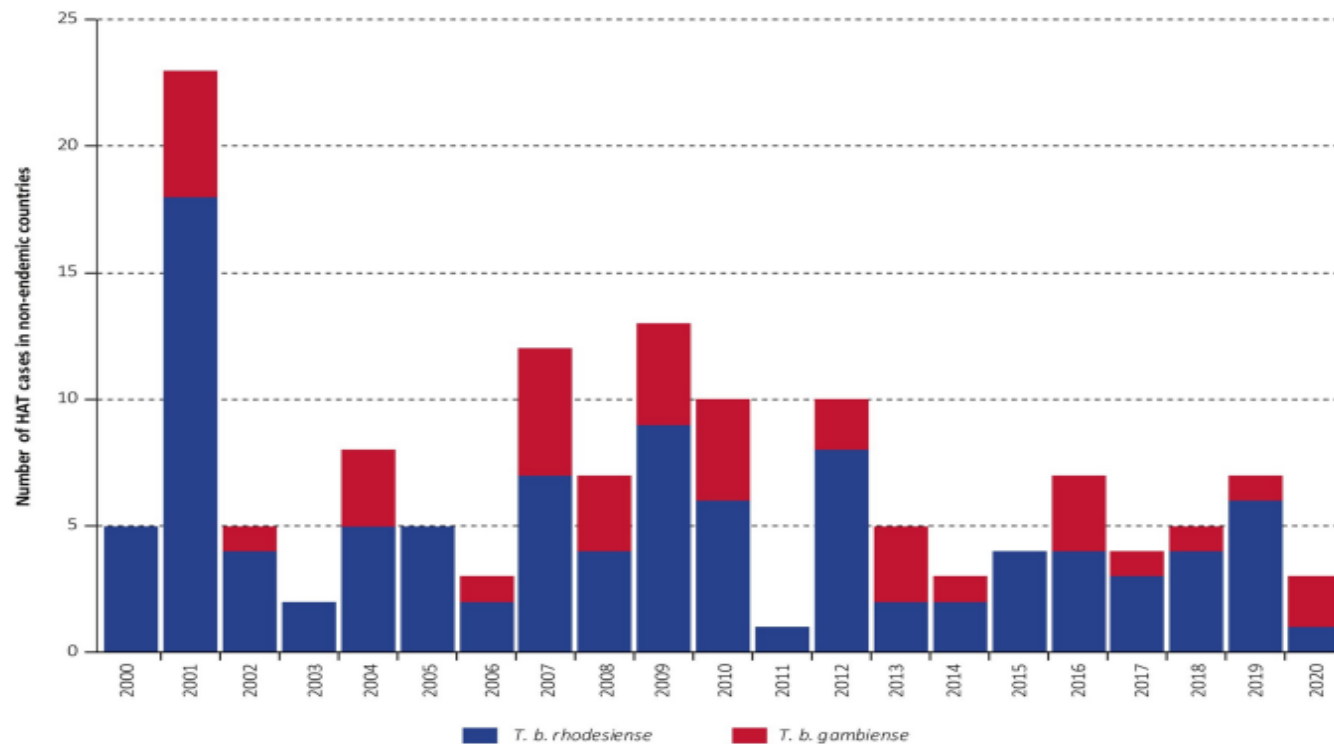


Fig 1. Cases of HAT detected in non-DEC. 2000–2020.

PLOS NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Human African trypanosomiasis cases diagnosed in non-endemic countries (2011–2020)

Jose R. Franco^{1*}, Giuliano Cecchi², Gerardo Priotto¹, Massimo Paone², Augustin Kadima Ebeja³, Pere P. Simarro⁴, Abdoulaye Diarra³, Dieudonné Sankara¹, Weining Zhao², Daniel Argaw Dagne¹

Journal of TRAVEL MEDICINE

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REVIEW

Human African Trypanosomiasis in Non-Endemic Countries (2000–2010)

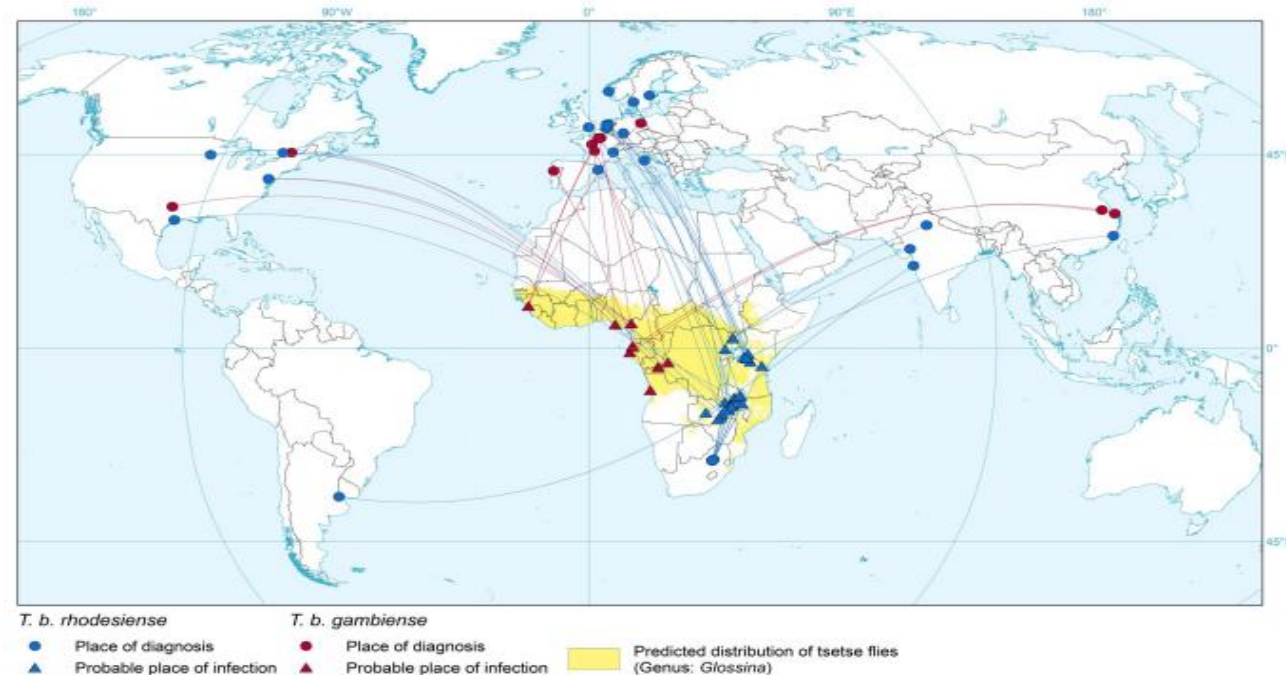
Pere P. Simarro, PhD,* José R. Franco, MD,* Giuliano Cecchi, MD,† Massimo Paone, MD,‡ Abdoulaye Diarra, PhD,‡ José A. Ruiz Postigo, PhD,§ and Jean G. Jannin, PhD*

HAT: cases in non-endemic countries

Exported cases of human African trypanosomiasis are reported from all continents,

- *T. b. rhodesiense* disease is mainly diagnosed in tourists, hunters or conservationist workers who have visited protected areas in Tanzania, Kenya, Malawi, Uganda, Zambia and Zimbabwe.
- *T. b. gambiense* is rare in tourists but appears in migrants, refugees, and long-term expatriates. Occasionally can appear long time after infection (e.g. 30 years).

Cases of human African trypanosomiasis in non-endemic countries (2011-2020)





Thanks for your attention !