Performance of diagnostic algorithms based on Rapid Diagnostic Tests to detect Sleeping Sickness in DR Congo

5th JOINT EANETT/HAT PLATFORM SCIENTIFIC MEETING
“Research and control activities challenges in keeping HAT below the elimination threshold beyond 2020”
KAMPALA, 3-4 OCTOBER 2018

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**Background**

- The prevalence of *Tbg* HAT has fallen

  ➢ HAT is targeted for elimination as PHP by 2020

  ➢ At low prevalence, cost-effectiveness of active case detection decreases

  ➢ Therefore integration of case finding into routine activities of peripheral health centres (PHC) becomes crucial.

  ➢ Adapted diagnostic tests and test algorithms required

• Opportunities for an effective integration into routine activities of PHC:

  ➢ The venue of individual rapid diagnostic tests (RDT) for of HAT screening:

    ✓ 1st generation RDT (native antigens): HAT Sero-K-set, SD Bioline HAT 1.0

    ✓ 2nd generation RDT (recombinant antigens): rHAT Sero Strip, SD Bioline HAT 2.0

  ➢ Serological (Trypanolysis, ELISA) and molecular (LAMP, RT-PCR) reference tests (RT) performed at national/regional reference centres

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Objectives

General objective:  
• To validate the performance of diagnostic tools and algorithms for diagnosis of *Tbg* HAT under conditions of passive case detection

Specific objectives: 
• To determine the diagnostic performance and costs for passive case detection in PHC in low prevalence HAT foci of:
  • HAT rapid diagnostic tests (RDT) performed on clinical suspects using fresh blood
  • combinations of HAT RDTs performed on clinical suspects using fresh blood
  • diagnostic algorithms of HAT RDTs on clinical suspects using fresh blood, with serological and/or molecular reference tests (RT) on filter paper (FP) at regional reference centres (INRB, Kinshasa, DR Congo)
Methodology - general

• This work in DR Congo is part of the DiTECT-HAT project

• Study Setting: Two levels of health centres
  • Serological Screening Sites (SSS): Clinical suspicion, perform RDT, refer RDT+ve to CDT
  • Centres for Diagnosis and Treatment (CDT): clinical suspicion, perform RDTs and parasitological confirmation of HAT, and treat HAT. Use of electronic case report forms.

• Inclusion criteria: Clinical suspicion of HAT

• Exclusion criteria
  • Previously treated for HAT
  • No informed consent
  • < 4 years old
Methodology: Procedures

- Inclusions started in October 2017
- Clinical suspects are tested with HAT-Sero-K-Set, SD Bioline HAT, rHAT Serostrip
- Participants with at least 1 RDT +ve result will undergo, at CDT:
  - Parasitological examination (lymph node fluid examination, mAECT ...);
  - Collection of blood on FP for reference tests (trypanolysis, LAMP, ELISA and real-time PCR)
  - Data-entry in a Personal Digital Assistant (PDA)
- RDT(s) +ve & Microscopy Trypano -ve subjects with 1 RT positive: microscopy parasitological testing at 3 and 6 months
- RDT(s) +ve & microscopy Trypano -ve subjects with all RT negative = considered as free of HAT
- For this presentation: Preliminary analyses based on PDA records only, inclusions until August 2018
Methodology: Procedures (2)

- HAT clinical symptoms
  + RDTs (in parallel)
  ×

Blood on filter paper

Parasitology

Reference tests

If + : 2x follow-up

+: HAT+

All -> HAT-

All -> go home
Results: enrolled participants characteristics

• 572 participants underwent RDT screening

• Excluded:
  • 18 participants no clinical sign suspecting HAT or missing clinical information
  • 9 participants with missing RDT results
  • 10 RDT+ participants with missing parasitological data

• 535 clinical HAT suspects enrolled (53.6% female, median age 26, IQR 17-42)
  • 15 referred from SSS to CDT
  • Persistent fever or headache reported respectively by 75% and 76% participants, both present for 63 % of participants.
  • Weight loss or weakness were positive for 31% and 29% of participants
  • Neurological signs were present for 28%
Results: Lab tests

• RDT results:
  • 427 (79.8%) participants negative in all RDTs (2 parasitology negative, 425 without parasitology results)
  • 108 (20.2%) positive in at least 1 RDT (RDT+)

• Parasitological results on RDT positives (at inclusion):
  • 25 confirmed HAT cases
  • 83 participants RDT(s) +ve but parasitology negative

• Reference Test (RT) results
  • 73 persons tested in RT out of 108 RDT+ (67.6%)
  • 39 RT positives out of 73 RT done
  • 19/25 confirmed HAT cases tested in RT, 19/19 RT positive
  • Among 20 RT+ and RDT+, only 6/20 underwent 2nd parasitological examination and 1 of them 3rd parasitological examination: 1 additional HAT case confirmed at 3 months and 1 at 6 months, bringing total number of detected HAT cases to 27.

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Results: Pictures for quality control

Camera on a microscope

Positive RDTs
Video of positive trypanosome sample at microscope

• 2_1_23_0136_1MA_20180715_121352.mp4
Sensitivity RDTs

• “N” = 27
  • 25 HAT cases at inclusion step
  • + 2 additional HAT cases at 3 and 6 months among positive RT participants

• “n” at 6 months, with RT results input:
  ✓ 27 +ve to HAT Sero-K-set,
  ✓ 16 +ve to rHAT Sero Strip
  ✓ 24 +ve to SD Bioline HAT 1.0 RDT
  ✓ 27 +ve to HAT Sero-K-set or rHAT Sero Strip, 27 +ve to HAT Sero-K-set or SD Bioline HAT 1.0, 26 +ve to rHAT Sero Strip or SD Bioline HAT 1.0, 27 +ve to at least one out of 3 RDTs

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<thead>
<tr>
<th>Test</th>
<th>Sensitivity (95% CI)</th>
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<tbody>
<tr>
<td>HAT Sero-K-set RDT</td>
<td>100% (87.2 – 100)</td>
</tr>
<tr>
<td>SD Bioline HAT 1.0 RDT</td>
<td>92.3% (74.9 – 99.1)</td>
</tr>
<tr>
<td>rHAT Sero Strip RDT</td>
<td>59.3% (38.8 – 77.6)</td>
</tr>
<tr>
<td>rHAT Sero Strip or SD Bioline HAT 1.0 RDTs</td>
<td>96.3% (81.0 – 99.9)</td>
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Specificity

- “N” (RDT negative (no parasitological confirmation or negative) plus RDT +ve (which remained parasitological negative)
  - **508** HAT controls at 6 months (2 with SD Bioline HAT 1.0 DT and rHAT Sero Strip RDTs not performed)
  
- “n”
  
  - **438** -ve to HAT Sero-K-set RDT, **494** -ve to rHAT Sero Strip RDT, **464** -ve to SD Bioline HAT 1.0 RDT, **435** -ve to both HAT Sero-K-set & rHAT Sero Strip RDTs, **398** -ve to both HAT Sero-K-set & SD Bioline HAT 1.0 RDTs, **427** -ve to both rHAT Sero Strip & SD Bioline HAT 1.0 RDTs, **397** -ve to both 3 RDTs

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<tr>
<td>rHAT Sero Strip RDT</td>
<td>97.6% (95.9 – 98.8)</td>
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<tr>
<td>SD Bioline HAT 1.0 RDT</td>
<td>91.5% (88.7 – 93.8)</td>
</tr>
<tr>
<td>HAT Sero-K-set RDT</td>
<td>86.2% (82.9 – 89.1)</td>
</tr>
<tr>
<td>rHAT Sero Strip &amp; SD Bioline HAT 1.0 RDTs</td>
<td>89.7% (86.6 – 92.3)</td>
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Discussions (1)

• Strengths
  • 3 RDTs in parallel. Probably very few HAT cases missed.
  • Photos of all RDT positives and videos of parasitology positives
  • Additional parasitological analysis on RT positives useful: allows confirmation of additional HAT cases

• Limitations
  • Low reference rates to CDT (15 referred from SSS to CDT in at least 9 months, as 1-2 suspects referred and received by a CDT): to be improved!
  • Low number of 2nd and 3rd parasitological investigation on RDT and RT positives: to be increased. As a result: specificity probably underestimated
  • SD Bioline HAT 2.0: foreseen but still not available
Discussions (2)

• Test performance
  • Sero-K-Set RT is the most sensitive, so far no statistical difference compared to SD Bioline 1.0 RDT
  • rHAT SeroS RDT is the most specific (difference statistical significant)

• Preliminary results only:
  • Inclusions will continue for at least 12 months
  • Only results registered in PDA so far. Many SSS RDT negatives still missing from the analysis and specificity calculations
  • Cost data will be included in final analyses

Training: enrolment simulation
• DiTECT-HAT is part of the EDCTP2 programme supported by the European Union (DRIA-2014-306-DiTECT-HAT)