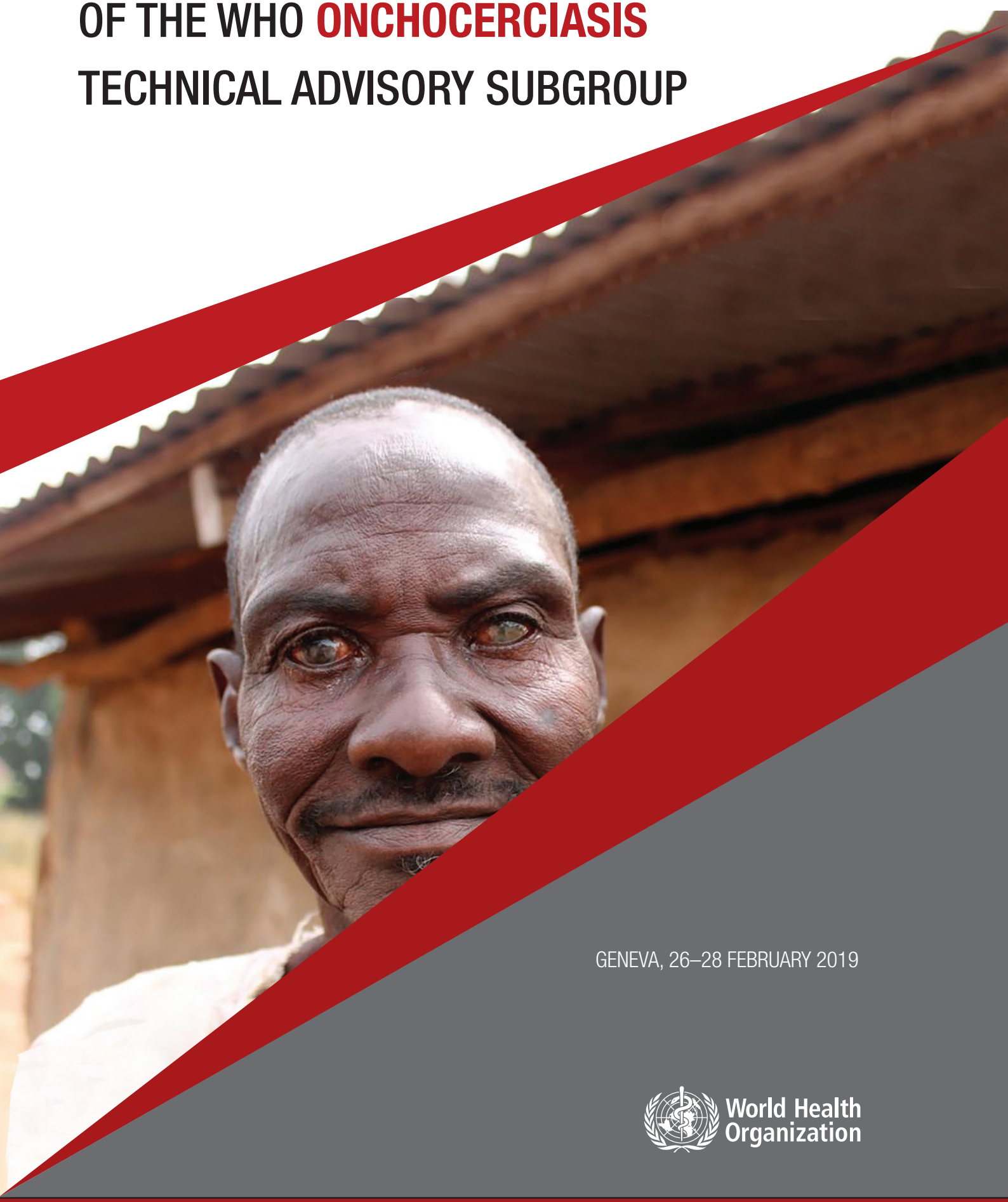
REPORT OF THE THIRD MEETING OF THE WHO ONCHOCERCIASIS TECHNICAL ADVISORY SUBGROUP



GENEVA, 26–28 FEBRUARY 2019

World Health Organization

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Abbreviations and acronyms

AP	alkaline phosphatase
APOC	African Programme for Onchocerciasis Control
CDC	United States Centers for Disease Control and Prevention
DBS	dried blood spots
ELISA	enzyme-linked immunosorbent assay
EPI	Expanded Programme on Immunization
HRP	horseradish peroxidase
LF	lymphatic filariasis
LGA	local government area
mAb	monoclonal antibody
MDA	mass drug administration
M&E	monitoring and evaluation
mf	microfilariae
NIH	United States National Institutes of Health
NOEC	national onchocerciasis expert committee
OD	optical density
OEC	onchocerciasis expert committee
OEPA	Onchocerciasis Elimination Program for the Americas
OTS	Onchocerciasis Technical Advisory Subgroup
PCR	polymerase chain reaction
PPES	probability proportional to estimated size
pre-TAS	pre-transmission assessment survey
PSU	primary sampling unit
PTS	post-treatment surveillance
QA	quality assurance
QC	quality control
RDT	rapid diagnostic test
REMO	rapid epidemiological mapping of onchocerciasis
SD	Standard Diagnostics
TAS	transmission assessment survey
TPP	target product profile
WHO	World Health Organization

Executive summary

The third meeting of the Onchocerciasis Technical Advisory Subgroup (OTS) of the World Health Organization (WHO) Department of Control of Neglected Tropical Diseases' Monitoring and Evaluation Working Group was held at WHO headquarters in Geneva, Switzerland, on 26–28 February 2019. The meeting reviewed new data comparing the available serological platforms for diagnosis of onchocerciasis and new data related to onchocerciasis elimination mapping (OEM). Additionally, it reviewed and provided input to the development of milestones relevant to elimination of onchocerciasis (interruption of transmission) for the achievement of the 2030 Sustainable Development Goals.

1. Comparison of available diagnostics

Data from a variety of settings and countries were examined to determine programmatically relevant performance characteristics. The major comparisons included:

- the Standard Diagnostics (SD) Bioline enzyme-linked immunosorbent assay (ELISA) kit;
- the United States Centers for Disease Control and Prevention (CDC) adaption of the alkaline phosphatase (AP) ELISA used by programmes in the Region of the Americas and in Ethiopia, Nigeria, Sudan and Uganda; and
- the SD Bioline rapid diagnostic test (RDT).

The version of the ELISA used in the Region of the Americas and in the aforementioned countries is referred to as the Onchocerciasis Elimination Program of the Americas (OEPA) ELISA in this report. In addition to reviewing results from a variety of field settings, a multi-site laboratory comparison of the available diagnostics that involved laboratories in the United States of America, Cameroon and Kenya took place. The comparisons of the available tests were challenging given the lack of a gold standard diagnostic and the paucity of other diagnostic data (e.g. skin snip polymerase chain reaction (PCR) or black fly PCR results). Generally, the SD Bioline ELISA kit yielded more positive results than the AP ELISA, which generally yielded more positive results that the SD Bioline RDT. Few comparisons involved the OEPA ELISA. There remained concerns that the SD Bioline ELISA kit yielded positive results that were not programmatically relevant because the discrepancy between the kit and the RDT was so large in many settings, and the too few positive results were based on results in several settings that had AP ELISA or other ELISA results.

Although all of the tests have been evaluated previously with specificity panels and have shown to be highly specific, some unanticipated false–positive results were obtained in samples from areas in which onchocerciasis is not endemic. The programmatic relevance of this was unclear at this time; the OEPA ELISA platform has been used in both the Region of the Americas and in the aforementioned countries without the level of cross-reactivity in the evaluation presented.

Test performance is not the only factor in deciding which test to use: the cost of the test, the logistics of procurement, the ease of quality assurance and quality control (QA/QC), and the reproducibility and standardization of results are also important. Data are being collected on all of these important considerations so that an informed decision can eventually be made. Regardless of the challenges, the ELISA has been used in a variety of formats and settings to demonstrate the impact of ivermectin treatment, to identify programmatic areas that are performing well and not well and to meet the WHO criteria for stopping mass drug administration (MDA).

As many programmes wish to proceed with OEM) it was important to try to find a way forward. Experiments demonstrated improved performance of the SD Bioline Ov16 RDT using blood eluted from dried blood spots (DBS) rather than from whole blood collected in the field. Finally, preliminary data from a new dual antigen test strip for onchocerciasis were reviewed. The addition of a second antigen (OvOC3261) to a lateral flow assay allowed identification of skin snip positive individuals who were missed by anti-Ov16 antibody response.

Recommendations

- Insufficient data are available for a recommendation of one ELISA platform over another. Programmes should continue to use the ELISA that they prefer; a QA system should be implemented and those data shared transparently with national onchocerciasis elimination committees to ensure that their decisions are based on the best available data.
- For OEM, DBS should be collected for mapping. Programmes could proceed with mapping using ELISAs or RDTs performed using blood from eluted DBS in a laboratory setting. Additional work is needed to define the performance of RDTs using blood from eluted DBS and provide recommendations for appropriate QA/QC.
- Additional ELISAs should be compared, including additional comparisons of the OEPA ELISA, and more data collected on intra- and interlaboratory variability in results. The unexpected false–positive results should be explored further. Until then, countries should continue to use the ELISA they prefer to evaluate when to stop MDA. Robust QA/QC systems should be implemented.
- The preliminary results of the new dual antigen test strip are encouraging; new tests that are better suited to programmatic needs, as specified by WHO, should be developed as a priority.

2. *Onchocerciasis elimination mapping*

Data from a variety of pilot survey of first stage of OEM were discussed, and presentations were given on the statistical considerations that should be included in determining the target threshold for starting MDA.

Recommendations

1. Exclusion mapping (i.e. identification of unmapped areas where the environment is unfavourable for the presence of black flies) is important and should be undertaken before proceeding to stage 1 mapping.
2. Mapping should begin in high-risk areas (e.g. in areas near hyper- and meso- endemic districts or in areas where onchocerciasis was found during previous surveys). National programmes may wish to delay OEM in areas at lower risk until more data from pilot surveys become available.
3. Stage 1: Purposeful sampling of first-line villages
    a. Select five first-line (or high-risk) villages.
    b. Draw a convenience sample of 100 adults.
    c. Test using eluted DBS on RDTs if programmes have insufficient experience with ELISA; save left over DBS. If ELISA is used, the QA/QC procedures should be properly documented and the results recorded.
    d. If Ov16 prevalence in one or more villages exceeds the statistical threshold, then initiate MDA.
    e. If Ov16 prevalence in all sites is below the statistical threshold, then proceed to stage 2 as merited by context