Essential Medicines Committee, Ghana

- Identified new drugs/ items to be approved
- Assembled the evidence, GRADE
- Guided the Panel

Zinc for diarrhoea

WHO global rec'

Ghana panel

- Diarrhoea-few deaths
- Zinc deficiency rare
- Trials done in Asia

Not recommended

Artesunate for severe malaria

WHO global rec'

Ghana panel

- Few severe malaria cases
- No QA supply
- Health workers not familiar

Not recommended

PLOS MEDICINE

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HEALTH IN ACTION

Integrating Global and National Knowledge to Select Medicines for Children: The Ghana National Drugs Programme

David Sinclair, Martha Gyansa-Lutterodt, Brian Asare, Augustina Koduah, Edith Andrews, Paul Garner

Published: May 21, 2013 • https://doi.org/10.1371/journal.pmed.1001449

Analysis

WHO guidelines on fluid resuscitation in children: missing the FEAST data

BMJ 2014 ; 348 doi: http://dx.doi.org/10.1136/bmj.f7003 (Published 14 January 2014)
Cite this as: *BMJ* 2014;348:f7003

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KEMRI | Wellcome Trust

Evidence to Policy: Paediatric Guideline Panels' Meeting

Draft evidence based recor
severely sick children with
disease in children.

These recommendations w
was held from 15-19th A
organized in partnership w
Wellcome Trust Research
National Health Research,
makers and researchers fr

The meeting was also supported by Prof. Paul Garner and Dr. David Sinclair f

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UKaid
FLUIDS THERAPY PANEL
SAROVA WHITESANDS BEACH HOTEL. 16th April 2013

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Developing guidelines in low-income and middle-income countries: lessons from Kenya

Mike English,[1,2] Grace Irimu,[3] Rachel Nyamai,[4] Fred Were,[5] Paul Garner,[6] Newton Opiyo[7]

[1]Health Serviecs Unit, KEMRI-Wellcome Trust Research Programme, Nairobi, Kenya
[2]Nuffield Department of Medicine, University of Oxford, Oxford, UK
[3]Department of Paediatrics and Child Health, University of Nairobi, Nairobi, Kenya

ABSTRACT

There are few examples of sustained nationally organised, evidence-informed clinical guidelines development processes in Sub-Saharan Africa. We describe the evolution of efforts from 2005 to 2015 to support evidence-informed decision making to guide admission hospital care practices in Kenya. The approach

district hospitals. This targeting recognised that availability of specifically trained paediatricians was very low and that more than 50% of hospital deaths occurred within 24–48 hours of arrival.[5]

In table 1 and figure 1 we outline in a temporal sequence the evolution of the Kenyan guidelines' procedural and technical developments and wider

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INDEX-TB GUIDELINES

Guidelines on extra-pulmonary tuberculosis for India

Initiative of
Central TB Division
Ministry of Health and Family Welfare, Government of India

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Phase 1. Initiation and scoping

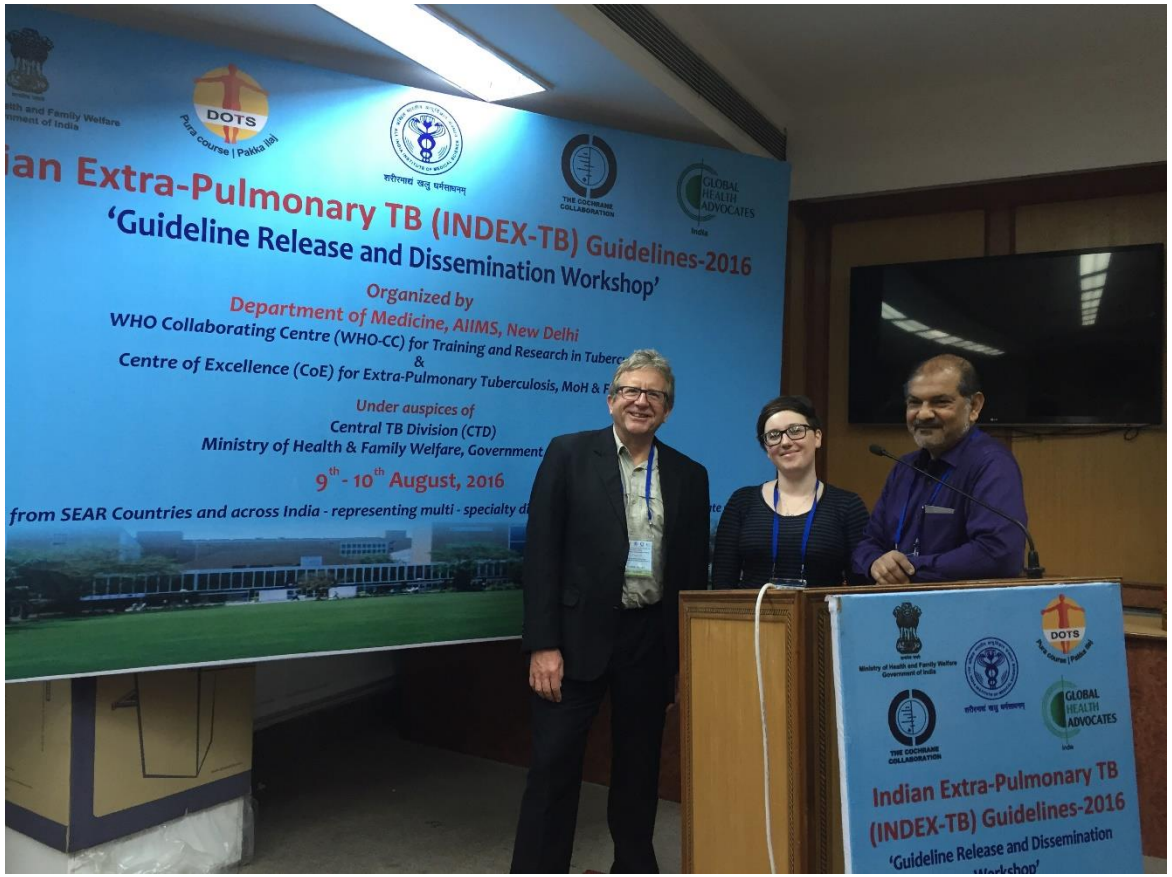
Central government initiated

.

Medical colleges draft clinical guides across twelve organ systems (6 months)

Cross-speciality meeting to initiate guidelines (1 week)

Table 2. Structures established in the first phase
Core committee The major stakeholders from India with clinical and scientific expertise in EPTB or with methodological expertise with evidence synthesis and guidelines development or national program implementation expertise. This group established the methods protocol; was responsible for the selection of the all other committees. They oversaw the writing, finalization after respond of peer review, and dissemination of the guidelines.
Technical Advisory Committee Expert clinicians, methods experts, public health officers, and representatives of the Government of India and WHO SEARO who contributed to prioritising research questions and evaluating the evidence base. Members of the TAC were selected to maximize diversity, relevant expertise, and representativeness of stakeholders. The TAC is divided into multiple sub-committees to evaluate evidence on various EPTB sites (for example, ocular, spine, lymph nodes).
Guideline Review Group This comprised the core committee and two specialists from each of the 12 TAC subcommittees.
Peer Review Committee The Peer Review Committee is a group of national and international experts who were chosen by the Technical Advisory Committee and the Core Committee to advise on the content and recommendations, and suggest corrections of the draft manuscript of the guidelines.
Methodology Support Team The Methodology Support Team consisted of methodologists from the Cochrane Infectious Diseases Group, based at the Liverpool School of Tropical Medicine in the United Kingdom and the South Asia Cochrane Centre in Vellore. Their role was to support the Core Committee and the TAC in the process of guidelines development, and particularly to provide methodological advice and support in evidence synthesis for the guidelines; and to prepare evidence summaries.
A declaration of interest was collected for all members of the above committees


DOTS
Pura course | Pakka ilaj
ian Extra-Pulmonary TB (INDEX-TB) Guidelines-2016
'Guideline Release and Dissemination Workshop'
Organized by
Department of Medicine, AIIMS, New Delhi
WHO Collaborating Centre (WHO-CC) for Training and Research in Tuberc
&
Centre of Excellence (CoE) for Extra-Pulmonary Tuberculosis, MoH & F
Under auspices of
Central TB Division (CTD)
Ministry of Health & Family Welfare, Government
9th - 10th August, 2016
from SEAR Countries and across India - representing multi - specialty d
THE COCHRANE COLLABORATION
GLOBAL HEALTH ADVOCATES
Indian Extra-Pulmonary TB
(INDEX-TB) Guidelines-2016
'Guideline Release and Dissemination

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Professor M C MISRA
DIRECTOR
AIIMS, NEW DELHI - 110029
TOSHIBA

Phase 2. Guideline formulation

Final focused questions planned for GRADE guideline development and evidence required

Question	Organ systems	Evidence
Should GeneXpert MTB/RIF be used in diagnosis?	Lymph node TB TB meningitis Pleural TB	Existing systematic review 2013: subsequent studies identified and summarised; GRADE table based on 2013 meta-analysis
Should corticosteroids be used routinely?	TB meningitis TB pericarditis Pleural TB	All three existing Cochrane reviews were updated for the guideline
How long should ATT be given for treatment?	Lymph node TB Abdominal TB TB meningitis	Used RCTS and cohort studies: Rapid review (non-Cochrane) Rapid review (new Cochrane) Rapid review (new Cochrane)

INDEX-TB GUIDELINES

Evidence Summaries and Guideline Panel Decision Tables

Core Group Guideline Meeting

14-18 July 2015

This document contains

- The systematic reviews and GRADE assessments used at the Index-TB Guideline Panel in July 2015
- The Evidence to Decision tables that record the Panel's assessment and recommendations from this meeting

The main guidelines are documented in:

Ministry of Health and Family Welfare. Index-TB Guidelines: guidelines on extra-pulmonary tuberculosis for India. Central TB Division: World Health Organization Country Office for India, 2016.

This document was finalized on

14 August 2016

By the Writing Committee

Xpert MTB/RIF for the diagnosis of LNTB

Figure 2: Forest plot demonstrating the sensitivity and specificity for Xpert MTB/RIF for the diagnosis of LNTB across all included studies a) against culture as a reference standard; b) against a combined reference standard. Blue squares represent point estimates of sensitivity and specificity, and lines represent 95% confidence intervals.

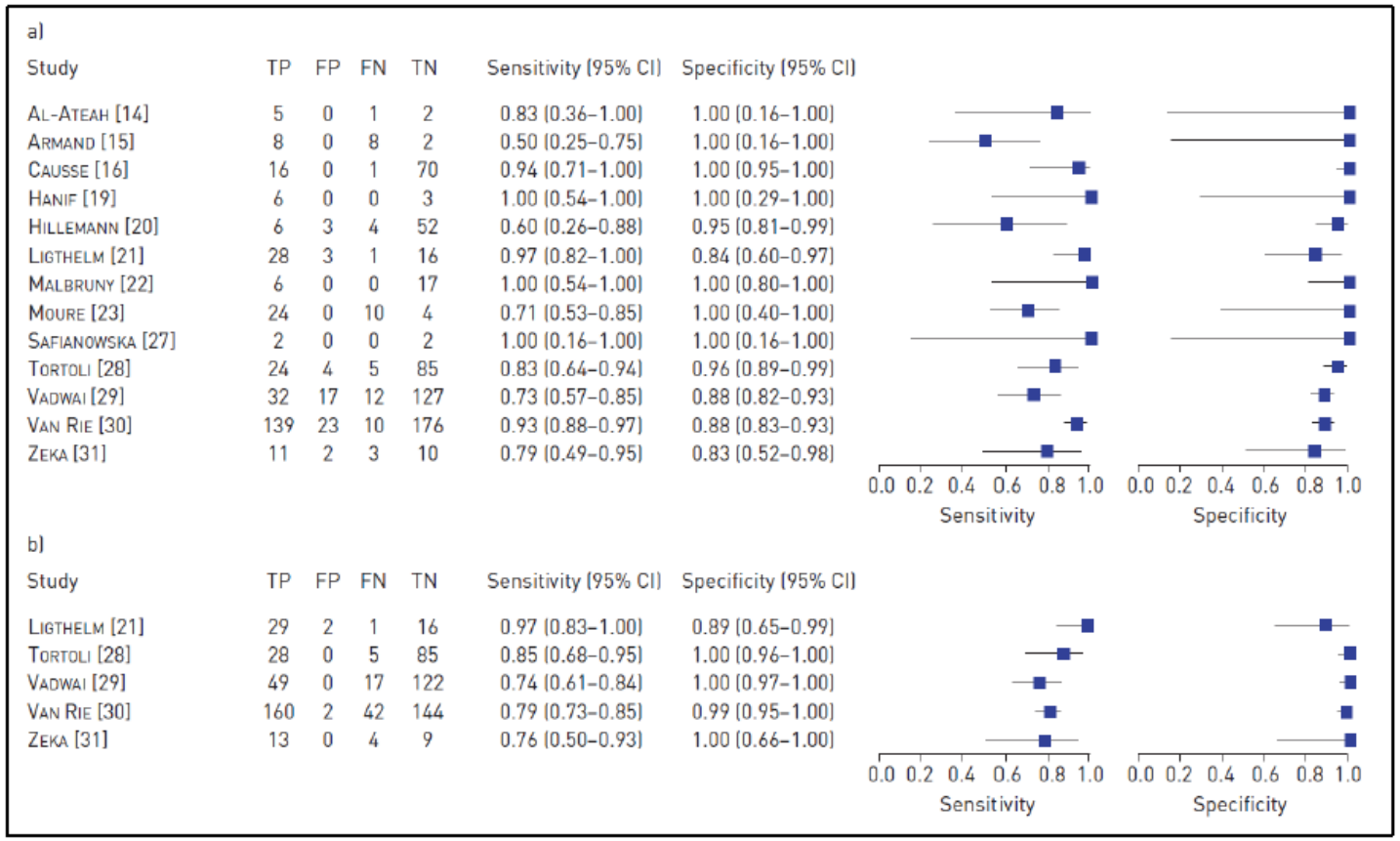

Table 1: Pooled sensitivity and specificity estimates for Xpert MTB/RIF for the diagnosis of LNTB against culture and against a combined reference standard.

	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)
Against culture	83.1% (71.4–90.7)	93.6% (87.9–96.8)
Against CRS	81.2% (72.4–87.7)	99.1% (94.5–99.9)

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Table 2: Should Xpert MTB/RIF be used to diagnose LNTB in patients suspected of LNTB?

Specimen: Lymph node aspirate and/or biopsy

Reference test: Culture

Sensitivity	0.83 (95% CI: 0.71 to 0.91)
Specificity	0.94 (95% CI: 0.88 to 0.97)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease quality of evidence					Effect per 1000 patients/year		Test accuracy QoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Pre-test probability of 20%	Pre-test probability of 45%	
True positives (patients with LNTB)	13 studies (362 patients)	Cohort & case-control type studies	Not serious [1]	Not serious [2]	Serious [3]	Serious [4]	Not serious	166 (142 to 182)	374 (320 to 410)	⊕⊕◯◯ LOW
False negatives (patients incorrectly classified as not having LNTB)								34 (58 to 18)	76 (130 to 40)	
True negatives (patients without LNTB)	13 studies (618 patients)	Cross-sectional (cohort type accuracy study)	Not serious [1]	Not serious	Not serious	Not serious	Not serious	752 (704 to 776)	517 (484 to 534)	⊕⊕⊕⊕ HIGH
False positives (patients incorrectly classified as having LNTB)								48 (96 to 24)	33 (66 to 16)	

1. Not downgraded for risk of bias: most studies were prospective cohort studies; only four of the thirteen studies were assessed as high risk of bias because patients were selected by convenience.
2. Not downgraded for indirectness: the studies were done in a variety of countries, mainly in secondary or tertiary centres and associated laboratories. The studies included mainly adults, but also children; HIV positive and negative people were included. The studies did not include specimens from patients being investigated for failed TB treatment/MDR TB.
3. Downgraded by one for inconsistency: unexplained heterogeneity may arise from differences between studies in specimen condition (fresh or frozen specimens), specimen processing and study population (e.g. prevalence of TB and HIV
4. Downgraded by one for imprecision: confidence intervals are wide partly due to the unexplained heterogeneity, and partly due to verification bias introduced by the imperfect reference standard.

Question: Should Xpert MTB/RIF be used to make a diagnosis of LNTB in addition to FNAC at district level?

Balance of desirable and undesirable effects

Desirable	Undesirable
Quicker diagnosis	Patients with false negative Xpert results may have ATT withheld or stopped in
May have fewer patients treated with ATT when they do not have LNTB	False negatives may go on to develop disseminated disease
Reduced stigma from reduction in overtreatment	False positives exposed to ATT unnecessarily
May identify rifampicin resistance (evidence unclear)	May falsely diagnose rifampicin resistance – harm to patient from SEs of 2nd lin
	Cost implications of managing missed cases (repeat diagnostic sampling, repea
	Stigma for patients given a false positive diagnosis
	Litigation for misdiagnosis

Overall quality of evidence across all critical outcomes

High	Moderate	Low	Very low
Specificity		Sensitivity	

Values and preference statement

LNTB is common and usually diagnosed and treated at primary/secondary care level. Needs rapid, accurate test to improve case de of treatment.

Draft recommendation

Xpert MTB/RIF should be used at district level as an additional test to FNAC in the diagnosis of LNTB.

Strength of recommendation

For intervention		No recommendation	Against intervention	
Strong	Conditional		Conditional	Strong
X				

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Table 5: Should Xpert MTB/RIF be used to diagnose TB meningitis in patients suspected of TB meningitis?

Specimen: Cerebrospinal fluid

Reference test: Culture

Sensitivity	0.81 (95% CI: 0.59 to 0.92)
Specificity	0.98 (95% CI: 0.95 to 0.99)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease quality of evidence					Effect per 1000 patients/year		Test accuracy QoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Pre-test probability of 2%	Pre-test probability of 10%	
True positives (patients with TB meningitis)	13 studies (185 patients)	Cohort & case-control type studies	Not serious [1]	Not serious [2]	Serious [3]	Serious [4]	Not serious	16 (12 to 18)	81 (59 to 92)	⊕⊕◯◯ LOW
False negatives (patients incorrectly classified as not having TB meningitis)								4 (8 to 2)	19 (41 to 8)	
True negatives (patients without TB meningitis)	13 studies (654 patients)	Cohort & case-control type studies	Not serious	Not serious	Not serious	Not serious	Not serious	960 (931 to 970)	882 (855 to 891)	⊕⊕⊕⊕ HIGH
False positives (patients incorrectly classified as having TB meningitis)								20 (49 to 10)	18 (45 to 9)	

Table 4. Context and values: Examples of Core Committee shaping the evidence summaries

Topic	Draft evidence summary	Core Committee feedback	Evidence summary changes
TB pericarditis	Initial draft summarised effect estimates from one large sub-Saharan African trial which aggregated HIV positive and negative patients	HIV less prevalent in India, and likely to be strong effect modifier; request stratified analysis	Trial authors provide methodology support team with a fresh analysis stratified by HIV status
	Mortality critical outcome	Mortality not the problem: clinicians give steroids to reduce long-term disability and reduce need for surgical intervention.	Methodology support team obtain constrictive pericarditis stratified by HIV status
TB pleura	Critical outcome was disability	Critical outcome was chest X-ray changes, as steroids given to prevent long-term X-ray changes that could influence employability overseas	Methodology support team extract X-ray changes in more detail

Key components in the success of INDEX-TB

- **Political will and a desire by all stakeholders to adopt new methods for guideline development;**

  Methodological direction independent of the clinical specialists to guide the process;

  Evidence synthesis experts with dedicated time to assemble evidence summaries;

  A central core from government with authority overseeing the process.