

**McGill Summer Institute: Advanced TB Diagnostics**  
**June 18, 2019**



# **C-reactive protein: The Triage Test We've Been Looking For?**

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**University of Washington, Seattle, USA**



# Disclosures

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> I have no financial conflicts to disclose

# Clinical scenario

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- > A 35 year old, HIV-infected man is seen in clinic in South Africa to start antiretroviral therapy.
- > CD4 unknown – tested HIV+ today, blood sent for CD4, will not know result for ~5 days
- > **TB screen - 4 symptom** screen: pt denies cough, fever, night sweats; **endorses weight loss**
- > **Plan:** obtain sputum for Xpert, defer ART while ruling out TB
- > Unable to produce sputum
- > **Now what?**
  - Trial of empiric abx
  - ignore wt loss & start ART (what about TPT?)
  - send to hospital for CXR, sputum inductions, other investigations
  - \*risk of LTFU
- > Is there a better triage process to determine whether this person needs further investigation for TB?

# Triage test goal & targets

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- > Determine whether person needs further investigation for TB
- > “rule-out” test
- > High sensitivity
- > Moderate-high specificity
- > High negative predictive value
- > Want good confidence that a negative triage test is a true negative for TB → TB ruled out
  
- > Current triage test (HIV) : 4-question symptom screen

# TPP for Triage Test (TPP2)

Characteristic	Optimal	Minimal
Goal	<ul style="list-style-type: none"><li>• identify patients with any symptoms of or risk factors for active (pulmonary) TB</li><li>• rule-out disease or refer to confirmatory testing</li></ul>	
Sensitivity	<b>&gt;95% overall</b>	<b>&gt;90% overall</b>
Specificity	<b>&gt;80%</b>	<b>&gt;70%</b>
Time-to-result	<5 mins	<30 mins
Price	<US\$1	< US\$ 2
Instrument	Not needed	Small, portable, or handheld, <1 kg
Manual preparation of samples	Integrated or no manual preparation	only 2 steps
Setting	Community or village level or higher levels	Health post or primary health-care clinics or higher

# **Current triage test (HIV+): 4QSS**

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## > Not on ART:

Sensitivity: **89.4%**

Specificity: **28.1%**

## > On ART

Sensitivity: **51.0%**

Specificity: **70.7%**

# C-Reactive Protein

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- > CRP: What is it?
- > Why look at CRP for TB screening?
- > What is the evidence for CRP as a triage test?
- > Could CRP be implemented today as a triage test for TB?



# A Sea of Blood Biomarkers

- N=55 persons with respiratory symptoms
- Mix of HIV+ and HIV-
- Ultimately categorized into TB or other respiratory disease
- 74 host biomarkers assayed at baseline
- 18 markedly different between TB and not TB

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Jacobs R et al *Oncotaraet* 2016

**Table 2: Median levels (and inter-quartile ranges in parenthesis) of host biomarkers detected in baseline plasma samples from pulmonary TB patients ( $n = 22$ ) and individuals with other respiratory diseases ( $n = 33$ ) and their diagnostic accuracies for TB disease.**

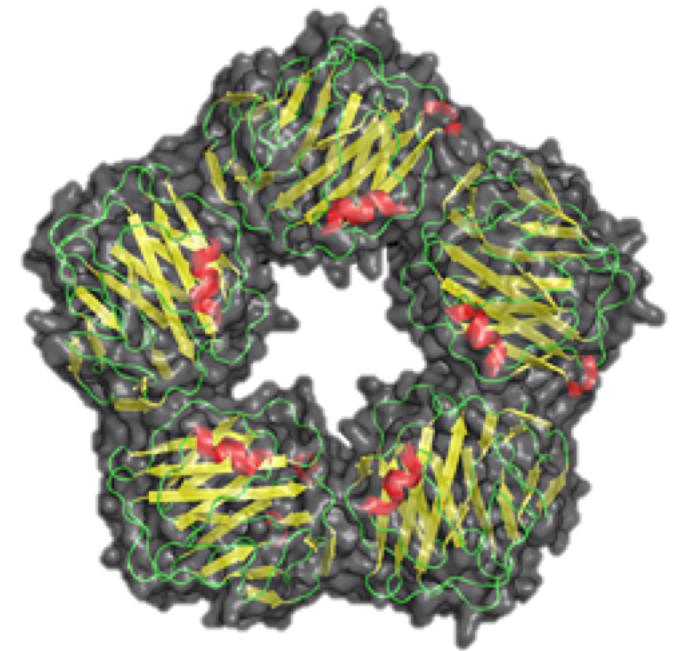
Marker	ORD (n = 33)	TB Disease (n = 22)	P value	AUC (95% CI)	Cut-off value	Sensitivity % (95% CI)	Specificity % (95% CI)
ADAMTS-13	3297(2569-4504)	4235 (2766-8073)	0.044	0.66 (0.51- 0.81)	> 3466	68 (45-86)	64 (45-80)
Antithrombin III	803100 (624200-968800)	625700 (519000-714300)	0.01	0.70 (0.56- 0.84)	<744162	91 (71-99)	61 (42-77)
Apo A-1	431400 (334100-548700)	274300 (242800-351500)	0.0014	0.76 (0.62- 0.89)	< 318930	73 (50-89)	82 (65-93)
BDNF	5774 (3824-8838)	3791 (1683-6187)	0.017	0.69 (0.55-0.84)	< 3467	45 (24-68)	91 (76-98)
CC4	114800 (70110-176600)	151600 (95100-291100)	0.100	0.63 (0.48- 0.79)	> 212263	32 (14-55)	97 (84-100)
CFH	729100 (557000-795100)	875400 (715200-980300)	0.0072	0.72 (0.57- 0.86)	> 808359	68 (45-86)	82 (65-93)
CRP	2019 (440-6330)	52980 (10020-137400)	P<0.0001	0.89 (0.79 -1.00)	> 9081	82 (60-95)	90 (76-98)
Ferritin	62850 (41840-120100)	161000 (116800-355300)	P<0.0001	0.78 (0.64 - 0.92)	> 93785	91 (71-99)	67 (48-82)
GDF-15	19.2(9.8-41.7)	49.24 (25.10-125.5)	0.002	0.75 (0.62 - 0.88)	> 21.06	91 (71-99)	55 (36-72)
HCC1	108000 (73120-130200)	144100 (108500-171800)	0.0022	0.75 (0.61- 0.89)	> 136956	59 (36-79)	85 (68-95)
I-309	1.24(1.1-1.4)	2.25 (1.4-3.5)	0.0002	0.80 (0.67- 0.93)	> 1.945	68 (45-86)	90 (73-98)
IFN- $\gamma$	5.78(0.39-49)	31.06 (8.81-156)	0.02	0.69 (0.54 - 0.83)	> 3.910	91 (70-99)	48 (31-66)
IL-33	88.77 (21.75-211.5)	164.9 (70.79-251.9)	0.100	0.63 (0.48- 0.78)	> 131.8	68 (45-86)	61 (42-77)
IP-10	444 (258-876)	1469 (878-3865)	P<0.0001	0.78 (0.64 - 0.91)	> 746.6	86 (65-97)	73 (54-87)
ITAC	628.0 (87.49-1253)	1106 (519.1-2042)	0.022	0.68 (0.54-0.83)	> 276.5	95 (77-100)	36 (20-55)
Lipocalin-2	453.9 (300.5-567.3)	600.7 (346.7-1028)	0.062	0.65 (0.50- 0.80)	> 552.8	59 (36-79)	76 (58-89)
MIG	312.4 (87.21-1028)	3076 (592.2-13830)	P<0.0001	0.81 (0.69- 0.94)	> 1700	68 (45-86)	88 (72-97)
MIP-4	92.5 (53.6-152)	208 (90-369)	0.012	0.70 (0.55- 0.85)	> 220.9	50 (28-72)	91 (76-98)
NCAM	592100 (430200-684200)	350800 (306800-421000)	P<0.0001	0.88 (0.78- 0.98)	< 477229	91 (71-99)	73 (54-87)
PCT	7520 (6749-8370)	8702(8185-9888)	0.0009	0.77 (0.64- 0.90)	> 8101	86 (65-97)	67 (48-82)
PEDF	10790 (8852-12870)	12360 (10360-15270)	0.0502	0.66 (0.50- 0.81)	> 11423	68 (45-86)	64 (45-80)
p-selectin	202(163-549)	441 (263-796)	0.030	0.67 (0.53 - 0.82)	> 265.7	77 (55-92)	58 (39-75)
SAA	5972(1324-12570)	9837 (6078-43000)	0.0081	0.71 (0.58 - 0.85)	> 8626	68 (45-86)	70 (51-84)
SAP	21850 (16980-24670)	30660 (23820-45050)	P<0.0001	0.85 (0.72-0.98)	> 25958	68 (45-86)	85 (68-95)
sFAS	5.3 (1.8-8.0)	8.03 (4.52-13.22)	0.065	0.65 (0.50- 0.81)	>6.7	67 (43-85)	68 (49-83)
TNF-a	7.4(4.1-13.4)	15.9 (11.8-24.6)	0.0024	0.74 (0.61- 0.88)	> 10.85	82 (60-95)	73 (54-87)
TPA	5895 (5187-6507)	7199 (6536-7702)	0.0002	0.80 (0.68- 0.92)	> 6307	86 (65-97)	76 (58-89)
Transthyretin	544700 (398000-638500)	293700 (212700-397500)	0.0005	0.78 (0.65- 0.91)	< 416242	82 (60-95)	76 (58-89)
VEGF	147 (0-546)	289 (134.3-877)	0.081	0.64 (0.50- 0.79)	> 175.6	73 (50-89)	55 (36-72)

Only analytes showing significant differences or trends between groups with the Mann-Whitney U test are shown. Optimal cut-off values and associated sensitivity and specificity were determined based on the Youden's Index. The concentrations of CRP, SAP, SAA, antithrombin III, ADAMTS-13, p-selectin, GDF-15, Apo A-1, transthyretin, CFH, sFAS, lipocalin-2, MIP-4 and CC4 are in  $\text{ng}/\text{ml}$ . The concentrations of all the other analytes are in  $\text{ng}/\text{ml}$ .

# C-reactive protein

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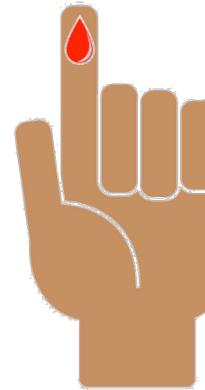
- > Nonspecific acute-phase serum inflammatory marker
- > Synthesized in response to IL-6
- > Hepatic production
- > Normal adult range 0.8-3 mg/L
- > Quickly (6-12 hours) elevates in setting of tissue damage, cytokine release, febrile illness



# How do you measure CRP?

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- > Lab-based assay (requires access to L3 lab)
  - Blood sample – venous draw (add on to other blood tests, e.g. blood count)
  
- > Point-of-care assays available
  - Capillary blood – fingerstick



# Nonspecific host

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> **Marker for numerous inflammatory conditions**

- Infection (bacterial >> viral)
- Autoimmune disease
- Vascular disease (MI, atherosclerotic disease)
- Trauma/burns/surgery
- Malignancy

> **Current clinical guidelines for CRP measurement use:**

- Monitor anti-inflammatory treatment
- Differentiate bacterial vs. viral febrile illness to determine need for abx
- Evaluate cardiovascular risk

# CRP is elevated in active TB

Short Report

**Serum C-reactive protein and detection of tuberculosis in persons co-infected with the human immunodeficiency virus**

**S. D. Lawn<sup>1,2</sup>, S. Wiktor<sup>3</sup>, D. Coulibaly<sup>3</sup>, A. N. Ackah<sup>3</sup> and R. B. Lal<sup>1</sup>** <sup>1</sup>HIV/AIDS and Retrovirology Branch and <sup>2</sup>Tuberculosis and Mycobacteriology Branch, Division of AIDS, STD, and TB Laboratory Research, Centers for Disease Control and Prevention, Public Health Service, US Department of Health and Human Services, Atlanta, Georgia, USA; <sup>3</sup>Projet Retro-CI and Centres Antituberculeux, Abidjan, Côte D'Ivoire



**Mean CRP (mg/L)**

TB+: 85.0

TB-: 4.0

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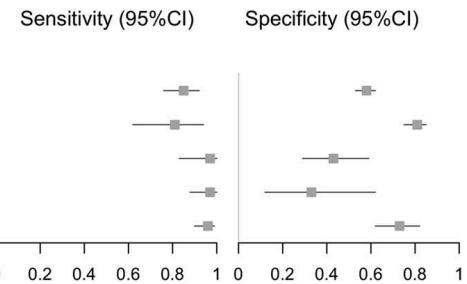
Lawn SD et al *Trans R Soc Trop Med Hyg* 2001



# Can CRP be used as a screening test?

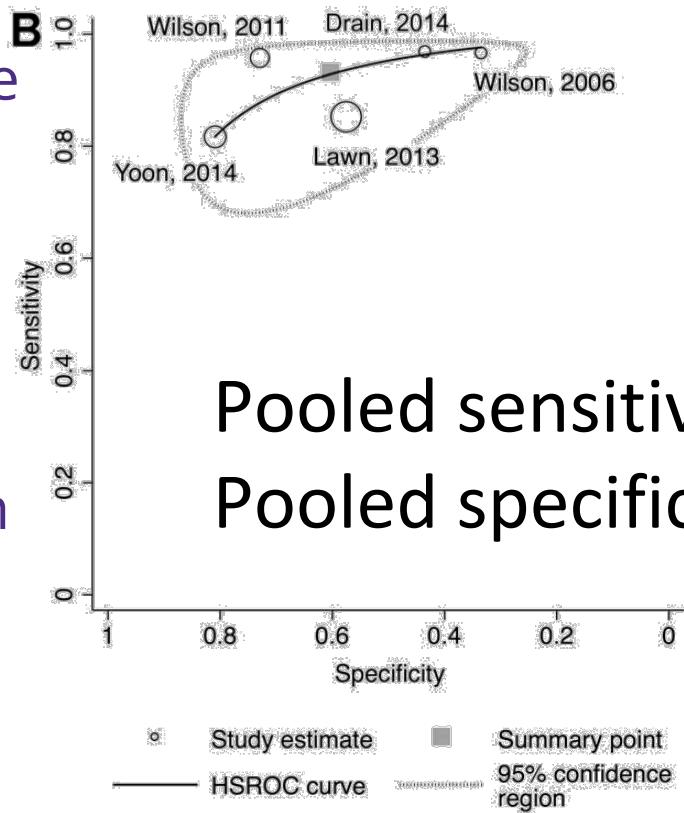
A

Study	TP	FP	FN	TN	Sensitivity (95%CI)	Specificity (95%CI)
*Lawn 2013 (S. Africa)	69	176	12	239	0.85 (0.76-0.92)	0.58 (0.53-0.62)
*Yoon 2014 (Uganda)	22	47	5	197	0.81 (0.62-0.94)	0.81 (0.75-0.85)
^Drain 2014 (S. Africa)	29	26	1	20	0.97 (0.83-1.00)	0.43 (0.29-0.59)
^Wilson 2006 (S. Africa)	57	10	2	5	0.97 (0.88-1.00)	0.33 (0.12-0.62)
^Wilson 2011 (S. Africa)	111	24	5	54	0.96 (0.90-0.99)	0.73 (0.62-0.82)



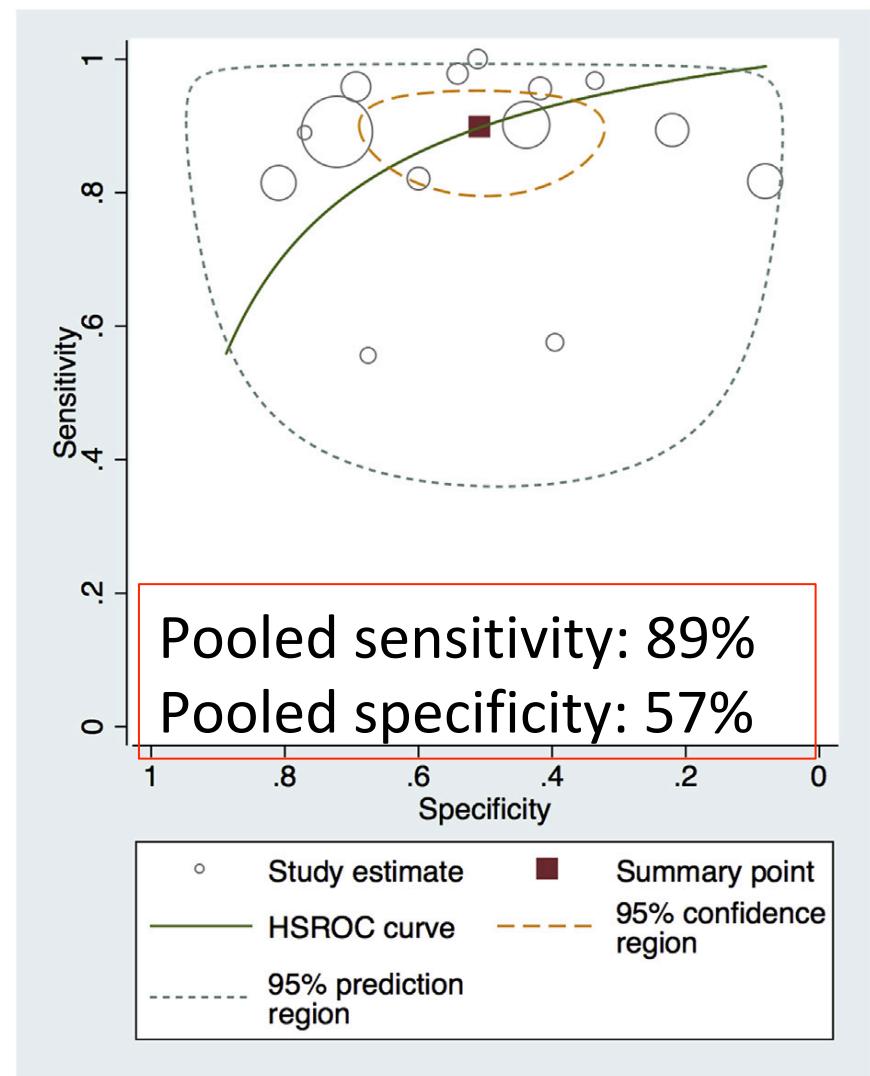
- > Systematic review & meta-analysis of CRP vs. TB culture
- > CRP threshold  $\geq 10\text{mg/L}$
- > Outpatients, mix of HIV+/-
  - High HIV burden settings
  - High TB burden settings
- > Mix of TB diagnostic evaluations (symptoms; high clinical suspicion) & routine screening scenarios

B



# CRP diagnostic accuracy for TB

- > Meta-analysis of 14 studies of CRP for TB dx
- > Includes more studies of HIV-negative only; low HIV-prevalence settings
  - China, India, South Korea, UK
- > Mix of hospitalized and outpatient cohorts, mix of lab & POC test
- > Variable CRP cutoff (5-12.5), most used 10mg/L



# Revisit WHO TPP

Characteristic	Optimal	Minimal	
Goal	<ul style="list-style-type: none"> <li>• identify patients with any symptoms of or risk factors for active (pulmonary) TB</li> <li>• rule-out disease or refer to confirmatory testing</li> </ul>		
Sensitivity	>95% overall	>90% overall	<input checked="" type="checkbox"/>
Specificity	>80%	>70%	<input checked="" type="checkbox"/>
Time-to-result	<5 mins	<30 mins	<input checked="" type="checkbox"/>
Price	<US\$1	< US\$ 2	<input checked="" type="checkbox"/>
Instrument	Not needed	Small, portable, or handheld, <1 kg	<input checked="" type="checkbox"/>
Manual preparation of samples	Integrated or no manual preparation	only 2 steps	<input checked="" type="checkbox"/>
Setting	Community or village level or higher levels	Health post or primary health-care clinics or higher	<input checked="" type="checkbox"/>

# Pros & Cons of CRP as a triage test

Pro	Con
Measurement gives objective value	Cost of measurement, device procurement, training/replacement
Point-of-care test available	Consistent for HIV +/- ? All CD4?
Rapid result <3mins	
Blood test (PTB & EPTB?)	
Low cost ~\$2-3/test	

## TB triage test in HIV+

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- > At the time of HIV testing, consideration of ART → Exclude active TB
- > Necessary for **immediate ART initiation** (goal)
- > Eligibility for **TB preventive therapy** initiation
- > 4SS inadequate
- > Need to have a test that works across CD4 count range
  
- > What about periodic screening after TB initially excluded?  
(e.g. picking up ART refills, return clinic visits)

# CRP as triage at ART initiation

## Point-of-care C-reactive protein-based tuberculosis screening for people living with HIV: a diagnostic accuracy study



Christina Yoon, Fred C Semitala, Elly Atuhumuza, Jane Katende, Sandra Mwebe, Lucy Asege, Derek T Armstrong, Alfred O Andama, David W Dowdy, J Luke Davis, Laurence Huang, Moses Kamya, Adithya Cattamanchi

- > 1237 Ugandan HIV+ adults, CD4<350
- > screened with 4QSS & POC CRP prior to initiating ART
- > Reference standard: TB culture & Xpert

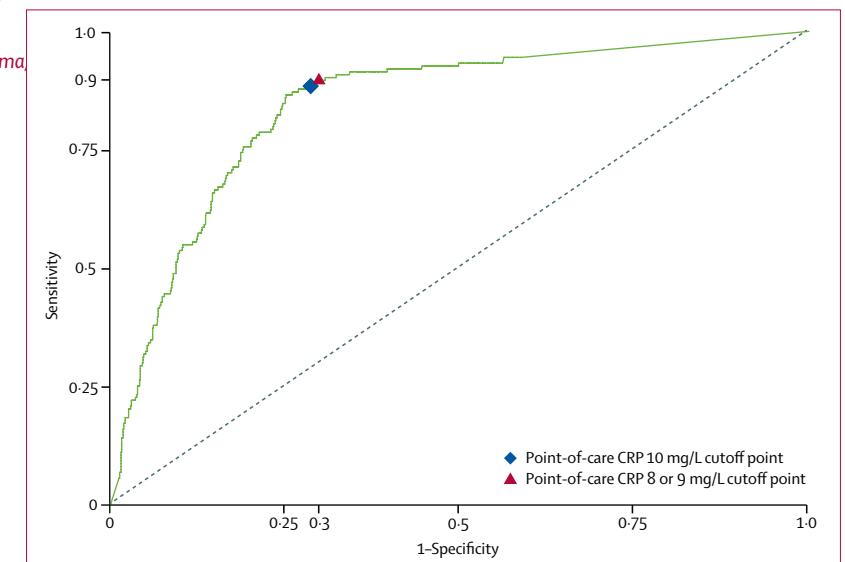


Figure 4: Receiver operating characteristic curves for the detection of culture-confirmed pulmonary tuberculosis by point-of-care CRP testing  
Area under the receiver-operating curve for 10 mg/L (0.81, 95% CI 0.78–0.83), 9 mg/L (0.81, 95% CI 0.78–0.83), and 8 mg/L (0.80, 95% CI 0.77–0.82) cutoff points. CRP=C-reactive protein

CRP cutoff	Ref standard	Sensitivity	Specificity
10	MGIT culture	89%	72%
10	Xpert	94%	
8-9	MGIT culture	>90%	>70%

# CRP screening in HIV+ outpatients

- > Test-and-treat → Triage test needs to have good performance across CD4
- > ART initiation cohort, South Africa, 2014-2015, median CD4=306 (IQR 176-468)
- > Lab-based CRP, TB reference: MGIT culture

**Table 2. Diagnostic characteristics of screening tests for tuberculosis in HIV-infected adults.**

Gold standard: TB culture	Sens % (95% CI)	Spec % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
(A) Diagnostic test properties of TB screening tests at selected cut-points: C-reactive protein (CRP), WHO 4-sympt				
CRP > 5	90.5 (77.4–97.3)	58.5 (53.4–63.5)	19.3 (14–25.5)	98.2 (95.6–99
CD4 <sup>+</sup> ≤ 200 (N = 127)	96.0 (79.0–99.0)	77.5 (71.5–83.5)	22.5 (14.5–31.5)	97.5 (86.8–99
CD4 <sup>+</sup> > 200 (N = 284)	80.0 (55.0–95.0)	72.5 (67.5–77.5)	22.5 (14.5–31.5)	93.4 (95.3–99
CRP > 10	78.6 (66.6–89.6)	72.5 (67.5–77.5)	22.5 (14.5–31.5)	95.9 (94.1–98
CRP > 50	47.6 (33.6–61.6)	72.5 (67.5–77.5)	22.5 (14.5–31.5)	94.0 (91–96.2
Any WHO symptom	90.5 (77.5–97.5)	72.5 (67.5–77.5)	22.5 (14.5–31.5)	97.3 (93.1–99
CD4 <sup>+</sup> ≤ 200 (N = 127)	92.0 (74.0–99.0)	72.5 (67.5–77.5)	22.5 (14.5–31.5)	92.0 (74.0–99
CD4 <sup>+</sup> > 200 (N = 284)	86.7 (59.5–98.3)	43.5 (37.5–49.6)	7.88 (4.26–13.1)	98.3 (94.1–99

CRP as triage would have reduced Xpert tests by 30-40% in this pop'n vs. symptom triage, same yield of TB

# POC CRP measurement tools



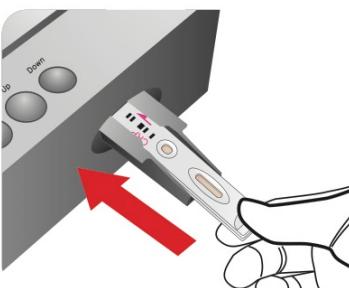
## Published evaluations for TB:

- > Nycocard (Alere)
    - Drain et al, IJTLD 2014 (+correlation with lab CRP)
  - > Afinion (Alere)
  - > iChroma (Boditech)
    - Yoon et al, JAIDS 2014
    - Yoon et al, Lancet ID 2017



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WHO Performance of Diagnostic Test																
Date of Data Entry/Update (DD/MM/YYYY)	Company Name	Company Size	Product Name	Product Type	Technology Type	Biomarker Type	Target Disease	Target Condition (linked to TPPs)	Health Level (lowest)	Status of R&D Project	Pathway Status	Targeted Market Entry (Regulatory Approval)	Certified QMS	Funder names	FND Portfolio	Website/Source
21.08.2017	Alere_Abon	Large	CRP Semi-Quantitative RTD	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	4-Regulatory achieved	No	NA		<a href="http://www.alere.com/content/en/abon.html">http://www.alere.com/content/en/abon.html</a>	
21.08.2017	Alere_Diagnostic Nord	Large	CRP rapid test (Ref. CRP-K10)	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	4-Regulatory achieved	Yes	NA		<a href="http://www.alere.com/content/en/abon.html">http://www.alere.com/content/en/abon.html</a> <a href="http://www.alere.com/content/en/abon.html?ref=CRP-K10">http://www.alere.com/content/en/abon.html?ref=CRP-K10</a>	
21.08.2017	Assure Tech	Large	Ecostest CRP RTD W23	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	4-Regulatory achieved	Yes	NA		<a href="http://www.assure.com">http://www.assure.com</a>	
21.08.2017	Biosynex	Large	Biosynex CRP Test Cassette (Ref. BCR0003)	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	4-Regulatory achieved	Yes	NA		<a href="http://www.biosynex.com/get-diagnostic-test-cards.aspx">http://www.biosynex.com/get-diagnostic-test-cards.aspx</a>	
21.08.2017	BTNX	Large	Rapid Cassette Protein CRP Test (Ref. 13240)	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	4-Regulatory achieved	Yes	NA		<a href="http://www.bnxtx.com">http://www.bnxtx.com</a>	
21.08.2017	Cortez Diagnostics	Medium	OneStep CRP Serum/Whole Blood Rapid Test/UnitTest	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	4-Regulatory achieved	Yes	NA		<a href="http://www.cortezdiagnostics.com/cortez/4-regulatory-approved-%25cdcb14c9-06e9-405a-960a-1685701015-15-15.pdf">http://www.cortezdiagnostics.com/cortez/4-regulatory-approved-%25cdcb14c9-06e9-405a-960a-1685701015-15-15.pdf</a>	
21.08.2017	Creative Diagnostics	Large	CRP Rapid Test Cassette (Ref. DT233)	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	3-Validation	No	NA		<a href="http://www.creativediagnostics.com/rapid-test-cassette-crp-dt233.html">http://www.creativediagnostics.com/rapid-test-cassette-crp-dt233.html</a>	
21.08.2017	Creative Diagnostics	Large	CDIA CRP semi-Quantitative Rapid Test Kit (Ref. DTSL-1602)	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	3-Validation	No	NA		<a href="http://www.creativediagnostics.com/semi-quantitative-rapid-test-cassette-crp-dtsl-1602.html">http://www.creativediagnostics.com/semi-quantitative-rapid-test-cassette-crp-dtsl-1602.html</a>	
21.08.2017	Getein Biotech	Large	One Step Test for HcRP + CRP	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LI Microscopy Center	Active	4-Regulatory achieved	Yes	NA		<a href="http://www.geteinbiotech.com/our-products/one-step-test-for-hcpr-and-crp.html">http://www.geteinbiotech.com/our-products/one-step-test-for-hcpr-and-crp.html</a>	
21.08.2017	Hogen Biotech	Large	UPTQuick CRP kit	Dx assay	Immunoassay	Protein	Fever	Bacterial versus non-bacterial differentiation test for fever	LD Community	Active	4-Regulatory achieved	Yes	NA		<a href="http://www.hogenbiotech.com/rapid-test-cassette-crp.html">http://www.hogenbiotech.com/rapid-test-cassette-crp.html</a>	



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<https://www.finddx.org/wp-content/uploads/2023/09/FindDX-Logo-2023-1024x1024.png>

# Cost-effectiveness

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- > **Uganda (HIV+, pre-ART):**
  - **CRP→Xpert algorithm:** same yield of TB, but >50% reduction of Xpert tests vs. **4QSS→ Xpert algorithm**  
(Yoon et al AJRCCM 2019)
- > Modeling study, simulated Ugandan population (HIV+/-):
  - Cough→CRP→Xpert algorithm is cost-effective in select populations/conditions:
    - > Background prevalence of TB ~5% (at least 2%)
    - > High risk of death from untreated TB (1% per month)
    - ICER: \$588/year of life gained

(Murray et al BMJ Global Health 2016)

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# Revisit WHO TPP: for HIV+ outpatients

Characteristic	Optimal	Minimal	
Goal	<ul style="list-style-type: none"> <li>• identify patients with any symptoms of or risk factors for active (pulmonary) TB</li> <li>• rule-out disease or refer to confirmatory testing</li> </ul>		
Sensitivity	>95% overall	>90% overall	<input checked="" type="checkbox"/>
Specificity	>80%	>70%	<input checked="" type="checkbox"/>
Time-to-result	<5 mins	<30 mins	<input checked="" type="checkbox"/>
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Instrument	Not needed	Small, portable, or handheld, <1 kg	<input checked="" type="checkbox"/>
Manual preparation of samples	Integrated or no manual preparation	only 2 steps	<input checked="" type="checkbox"/>
Setting	Community or village level or higher levels	Health post or primary health-care clinics or higher	<input checked="" type="checkbox"/>

## Revisit clinical scenario

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- > **Plan:** check POC CRP
- > **CRP = 3.5**
- > ***Low risk of active TB, high confidence***
- > No Xpert test needed
- > Initiate ART today
- > Initiate TB preventive therapy today
- > Follow up on schedule for refill, evaluation
- > Do we still need symptom screen?

- 35yo man, HIV+, CD4 unknown
- Sx: h/o weight loss
- No sputum

# **CRP as triage: review**

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- > **Meets TPP criteria to use in HIV+ adults, initiating ART**
- > Exceeds symptom screen performance
  - Replace symptom screen entirely?
- > Remaining questions:
  - For other populations will CRP be a good triage test?
  - Evidence/performance in HIV-uninfected? Low-incidence settings?
  - Optimal CRP threshold to use? 5? 10?
  - Performance in HIV+ on ART?
  - Frequency of repeat screening?
  - Performance in **children?**
- > **Good POC device options now;** new developments may improve cost, performance, portability

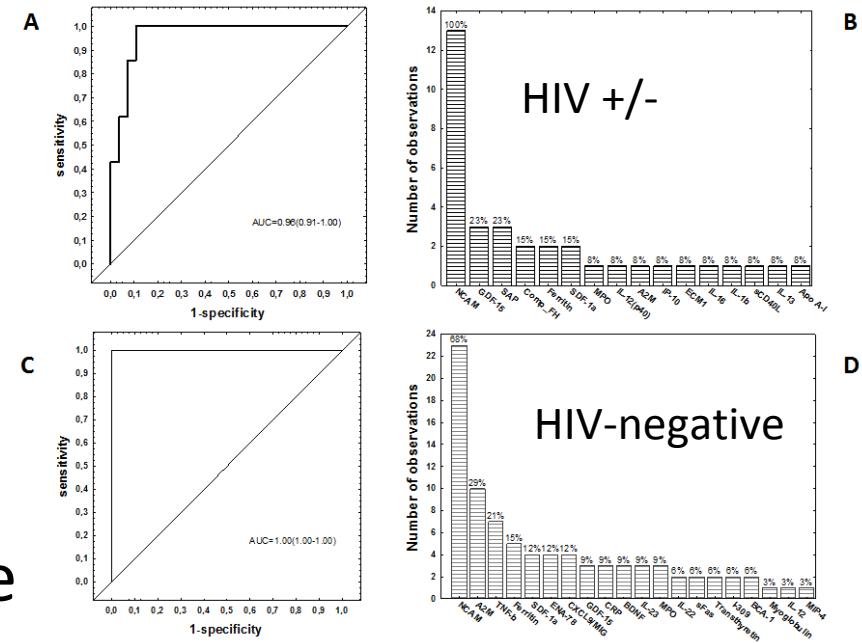
# CRP as triage

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- > **Setting-specific cost implications**
  - Need more research in other populations
- > **High-burden (TB/HIV) settings: likely high-use, cost-effective strategy to exclude TB → implement now!**
- > **Follow this space:**
  - Upcoming RCT (PI: Yoon, UCSF) in Uganda in HIV+ adults initiating ART
  - **Control:** symptom screen
  - **Intervention:** POC CRP
  - **Outcomes: TB diagnosed, IPT started, cost-effectiveness (incl. Xperts averted)**

# The future of CRP triage – back at sea ?

- 6-analyte panel to best correctly categorize TB+ or TB-
  - None contain CRP
  - Multi-marker signatures have better performance than single biomarkers
  - No current POC/NPOC platform to assay panels...yet



**Figure 2: Accuracy of multi-marker models in the diagnosis of TB disease.** Receiver operator characteristics (ROC) curve showing the accuracy of the most accurate six-marker biosignature (NCAM, SAP, IL-1 $\beta$ , sCD40L, IL-13 and Apo A-1) in the diagnosis of TB disease in all study participants, regardless of HIV infection status **A**, frequency of analytes in the top 13 general discriminant analysis (GDA) models that most accurately classified study participants as TB disease or ORD irrespective of HIV status **B**, ROC curve showing the accuracy of the most accurate six-marker biosignature (NCAM+A2M+IL-22+ferritin+ myoglobin+IL-12(p40) or NCAM+A2M+IL-22+ferritin+TNF- $\beta$ -MP-4) in the diagnosis of TB disease in HIV negative study participants **C**, and frequency of analytes in the top 34 GDA models that most accurately classified study participants as TB disease or ORD in the absence of HIV infection **D**. The bar graphs **B** and **D**, indicate the frequency of analytes in the most accurate GDA models.

# TB WARS

## EPISODE IV: A NEW HOPE



POC CRP is, in fact, the ~~droid~~ triage test you're looking for!\*

\*For HIV+, not on ART

# Questions

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# **Collaborators & Support**



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