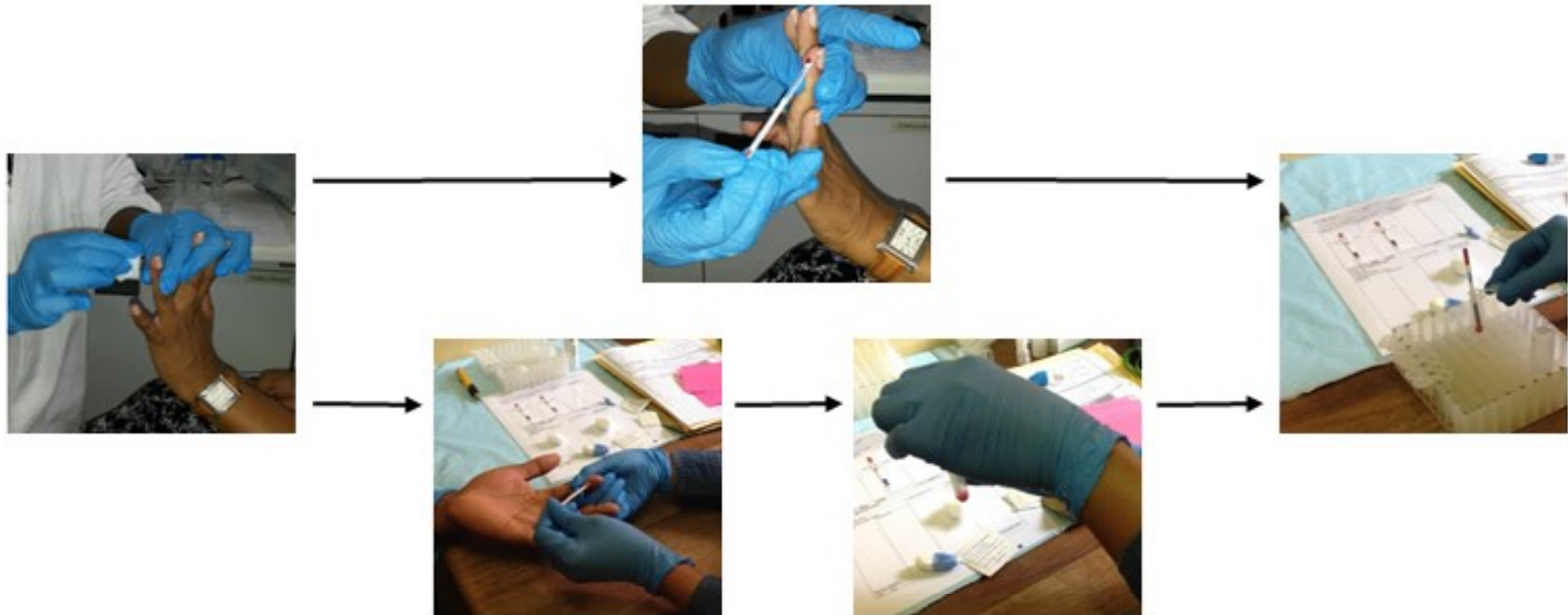











Direct application of LFA strip to finger-prick blood







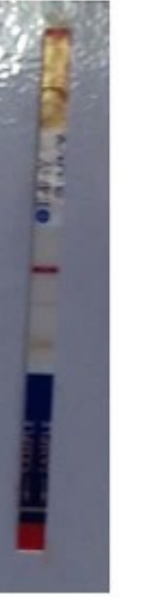
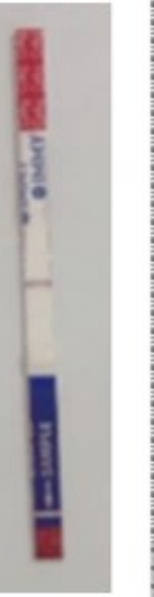



Pipetting finger-prick blood

Patient	1) 32M, CD4 8, no previous CM, not on ART, day 35 fluconazole, LP negative, alive & well at 6 months	2) 40M, CD4 64, no previous CM, ART 6 months, not on fluconazole, LP not done, alive & well at 6 months	3) 31F, CD4 9, no previous CM, LP negative, RIP 2 weeks (MAI)	4) 27M, CD4 71, no previous CM, on ART, LP negative, RIP 2 weeks (TB)	5) 34M, CD4 27, no previous CM, not on ART, day 3 fluconazole, LP negative, alive & well at 6 months	6) 33F, CD4 11, no previous CM, not on ART, day 4 fluconazole, LP negative, RIP 3 months (TB)	7) 28F, CD4 20, unknown previous CM, not on ART or fluconazole, LP not done alive & well at 6 months	8) 45M, CD4 31, no previous CM, not on ART, day 1 fluconazole, LP negative, alive & well at 4 months	9) 49M, CD4 17, no previous CM, defaulted ART, day 2 fluconazole, LP not done, alive & well at 4 months	11) 20F, CD4 29, no previous CM, not on ART, day 5 fluconazole, LP negative, alive & well at 5 months
Photo of IMMY CrAg LFAs performed on finger-prick blood (taken within 1 hour of reading)						Not available				
POC method	Direct application	Direct application	Direct application	Direct application	Direct application	Direct application	Direct application	Direct application	Direct application	Pipette transfer
(10 mins) (20 mins)	Negative Not done	Negative Not done	Negative Not done	Negative Not done	Negative Not done	Negative Not done	Negative Positive	Negative Positive	Negative Positive	Negative Positive
Plasma CrAg titer	10	40	5	<5	<5	10	<5	5	5	10

Supplementary Digital Content 2 Clinical details and photos of IMMY CrAg LFAs performed at POC, that were negative at POC but whose CrAg reference standard test was positive in a case-control diagnostic accuracy study. Nine patients had false negative results at POC when the IMMY CrAg LFA was applied directly to finger-prick blood and read after 10 minutes; however, of three whose tests were also read at 20 minutes, all became positive. None of six patients who had an LP performed had cryptococcal meningitis, and all had CrAg titers of ≤ 40 . The final false negative (11) was performed using a pipette to transfer finger-prick blood and was also read as positive at 20 minutes. CrAg titer was 10.

Abbreviations: M = male; F = female; CM = cryptococcal meningitis; ART = antiretroviral therapy; LP = negative; RIP = died; MAI = mycobacterium avium intracellulare; TB = tuberculosis.

Patient	1) 49F, CD4 19, no previous CM, vomiting, LP negative day 8, no fluconazole/ART, RIP day 25 with suspected CM	2) 28F, CD4 3, no previous CM, vomiting, headache, photophobia, LP negative day 51, received fluconazole (start date unknown), ART day 7, alive and well at 6 months	3) 37F, CD4 62, no previous CM, no symptoms, LP not done, received fluconazole (start date unknown), ART day 3, alive and well at 6 months	4) 34F, CD4 90, no previous CM, no symptoms, LP unknown, fluconazole/ART unknown, lost to follow up	5) 54M, CD4 104, previous CM, severe headache, photophobia, neck stiffness, LP declined but treated as presumed CM, ART day 3, lost to follow up	6) 49F, CD4 128, headache, vomiting, neck stiffness, photophobia, LP confirmed CM, treatment started day 0, ART day 14, alive & well at 1 month	2) 44M, CD4 79, no symptoms, no LP done, fluconazole started day 0, ART day 10, alive & well at 1 month	3) 43M, CD4 80, headache, photophobia, neck stiffness, LP declined, fluconazole day 0, ART not started due to contraindication, alive & well at 1 month	4) 35F, CD4 24, headache, photophobia, neck stiffness, vomiting, LP confirmed CM, treatment started day 0, ART unknown, alive & well 1 month
Photo of CrAg LFAs performed on finger-prick blood									
POC method	Direct application	Direct application	Direct application	Direct application	Direct application	Pipette transfer	Pipette transfer	Pipette transfer	Pipette transfer
POC result 0 mins 10 mins	Negative Negative	Negative Negative	Negative Negative	Negative Negative	Positive Positive	Positive Positive	Positive Positive	Positive Positive	Positive Positive
Plasma CrAg titre	10	Not done on fresh plasma (2560 on frozen & thawed blood)	40	20	160	2560	20	<5	2621440

Supplementary material Figure 2. Clinical details and photos of IMMY CrAg LFAs performed at point of care in the clinic-case implementation study for nine CrAg-positive patients. Four patients had false negative POC results using direct application of the LFA strip to finger-prick blood, CrAg titers performed on fresh plasma (3/4) were ≤ 40 and LPs performed were negative. One patient had a true positive result at point of care, CrAg titer 160. Four patients had true positive POC results using a pipette to transfer finger-prick blood to the diluent. Two had CrAg titers of ≤ 20 , and the other two had high titers and were diagnosed and treated for cryptococcal meningitis on the same day as screening.

Abbreviations: M = male; F = female; CM = cryptococcal meningitis; ART = antiretroviral therapy; LP = negative; RIP = died; MAI = mycobacterium avium intracellulare; TB = tuberculosis.