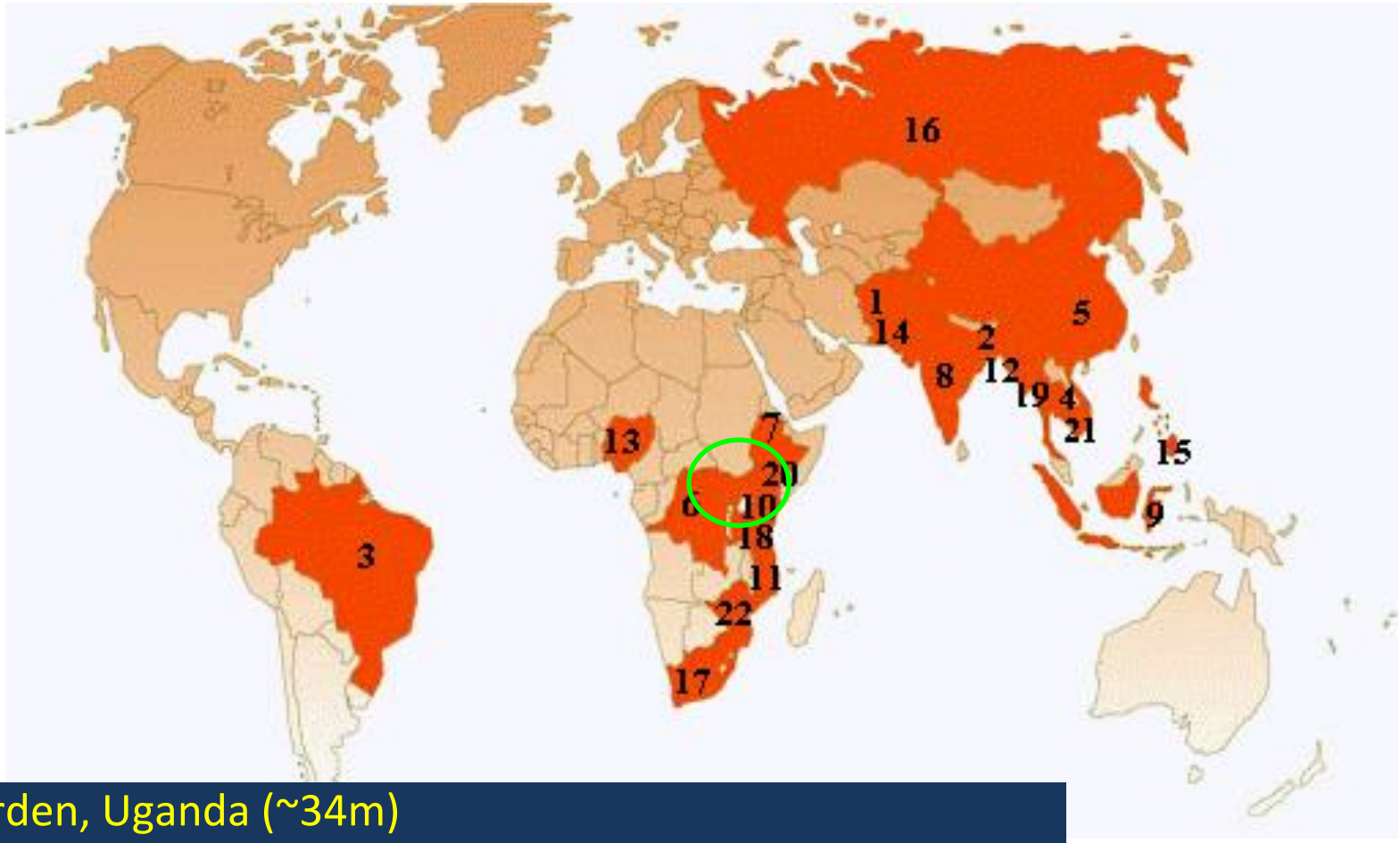
Surveillance of TB Drug Resistance: Lessons from Uganda

Moses Joloba

The 22 TB high Burden countries - WHO



TB Burden, Uganda (~34m)

- Ranked No. 16
- All forms of TB per year: **49,000** cases
- Mortality from all forms of TB: 29,000
- High HIV prevalence (6.4% POPn and 50% in TB patients)

Trend in Prevalence of MDR-TB in Uganda

Study	New	Previously treated
1996 –7 Survey in 19 districts in Uganda. (Bretzel et al, Int J Tuberc Lung Dis. 1999)	0.5%	4.4%
2008 – Kampala (Capital City) Drug Survey. (Lukoye D et al, PLoS ONE 6(1): e16130. 2011)	1.1%	11.7%
2010 – National Drug Survey (Manuscript in preparation)	1.4%	12.1%

Factors associated with MDR-TB in Uganda

Factor	Univariate			Multivariate		
		N (%)	95% CI		OR (95% CI)	P-value
Sex	Male	21/881 (2.4)	0.94 (0.4-2.0)		1.2 (0.50-3.30)	0.7
	Female	10/444 (2.3)				
Age	>35 years	22/568(3.9)	3.3 (1.5-7.0)	0.001	2 (1.0-4.3)	0.04
	<35 years	9/757 (1.2)				
Residence	Urban	28/798 (3.51)	6.3 (1.9-20.9)	0.002	6.0 (1.44-25.3)	0.02
	Rural	3/527 (0.57)				
HIV status	Positive	11/388 (2.8)	1.3 (0.6-2.6)	0.5		
	Negative	20/984 (2.2)				
Previous TB RX	Yes	14/116 (12.1)	8.6 (4.3-16.9)	<0.001	8.6 (4.0-18.2)	<0.001
	No	17/1209 (1.4)				

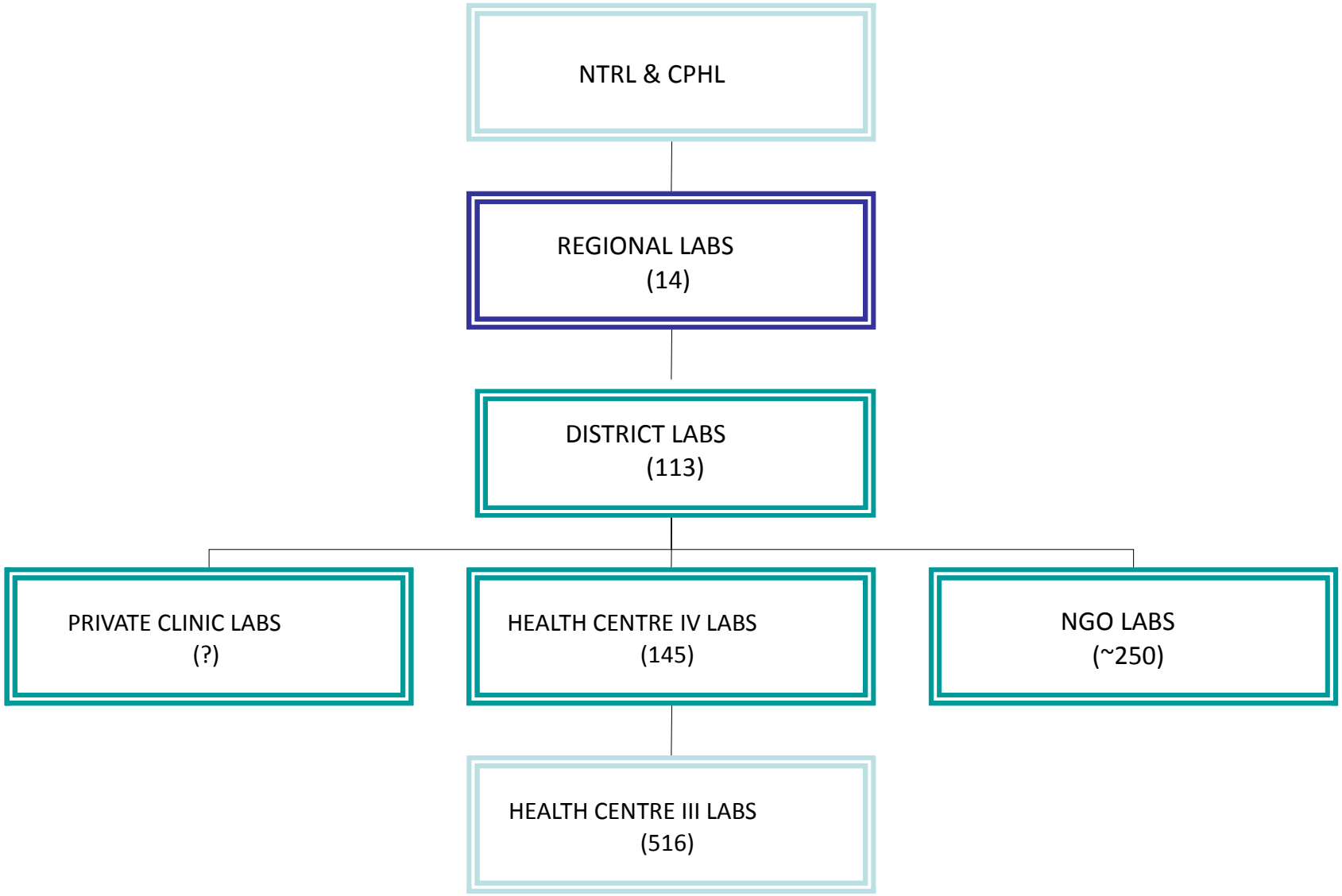
MDR TB Surveillance in Uganda

Factors leading to improved surveillance

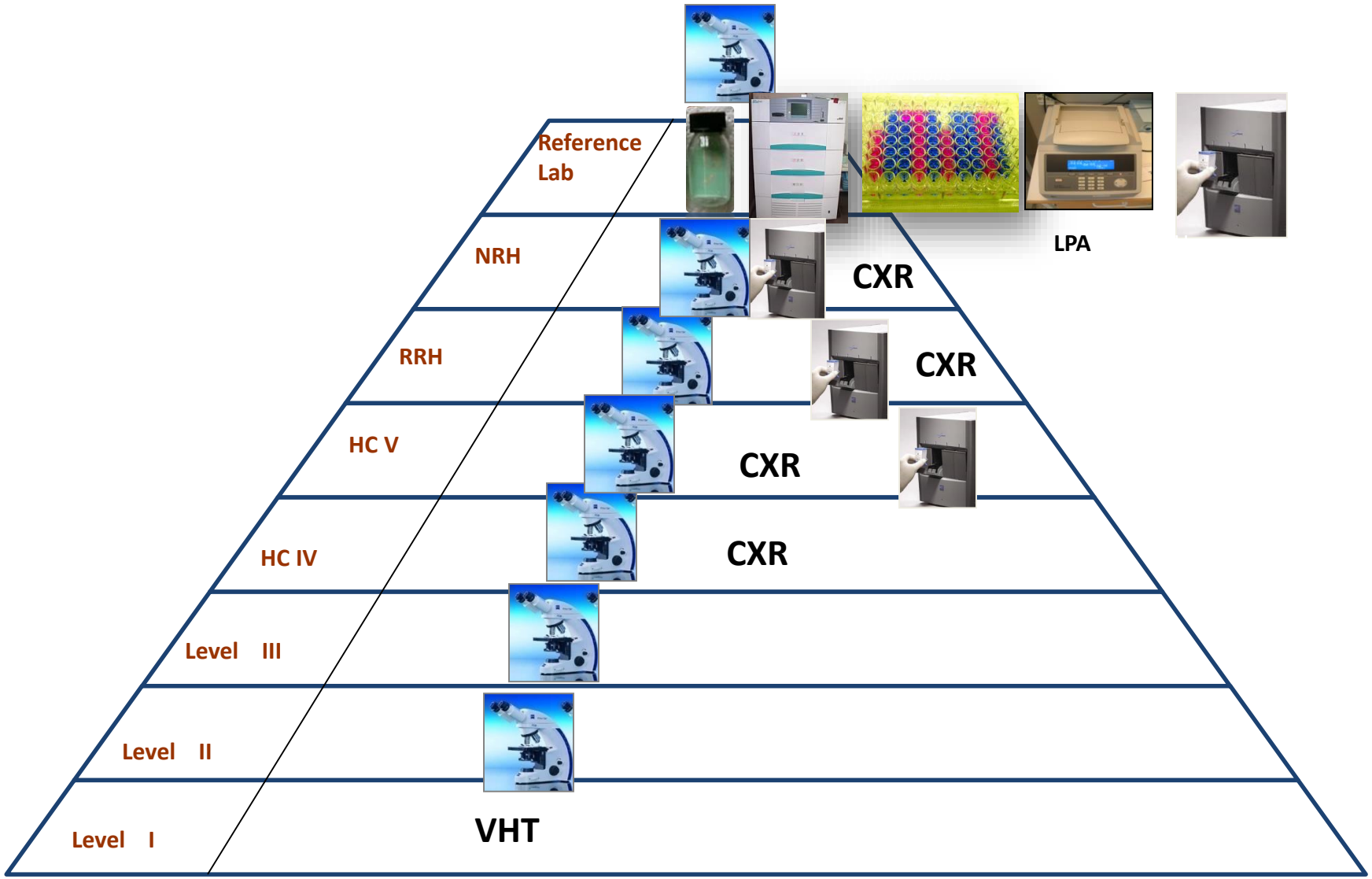
- Good sample referral system
- Improved diagnostics
- Use of supportive tools
  - Laboratory Information System (LIS)
  - Geographical Information System (GIS)
  - Electronic delivery of results (sms, e-mail, phone calls)

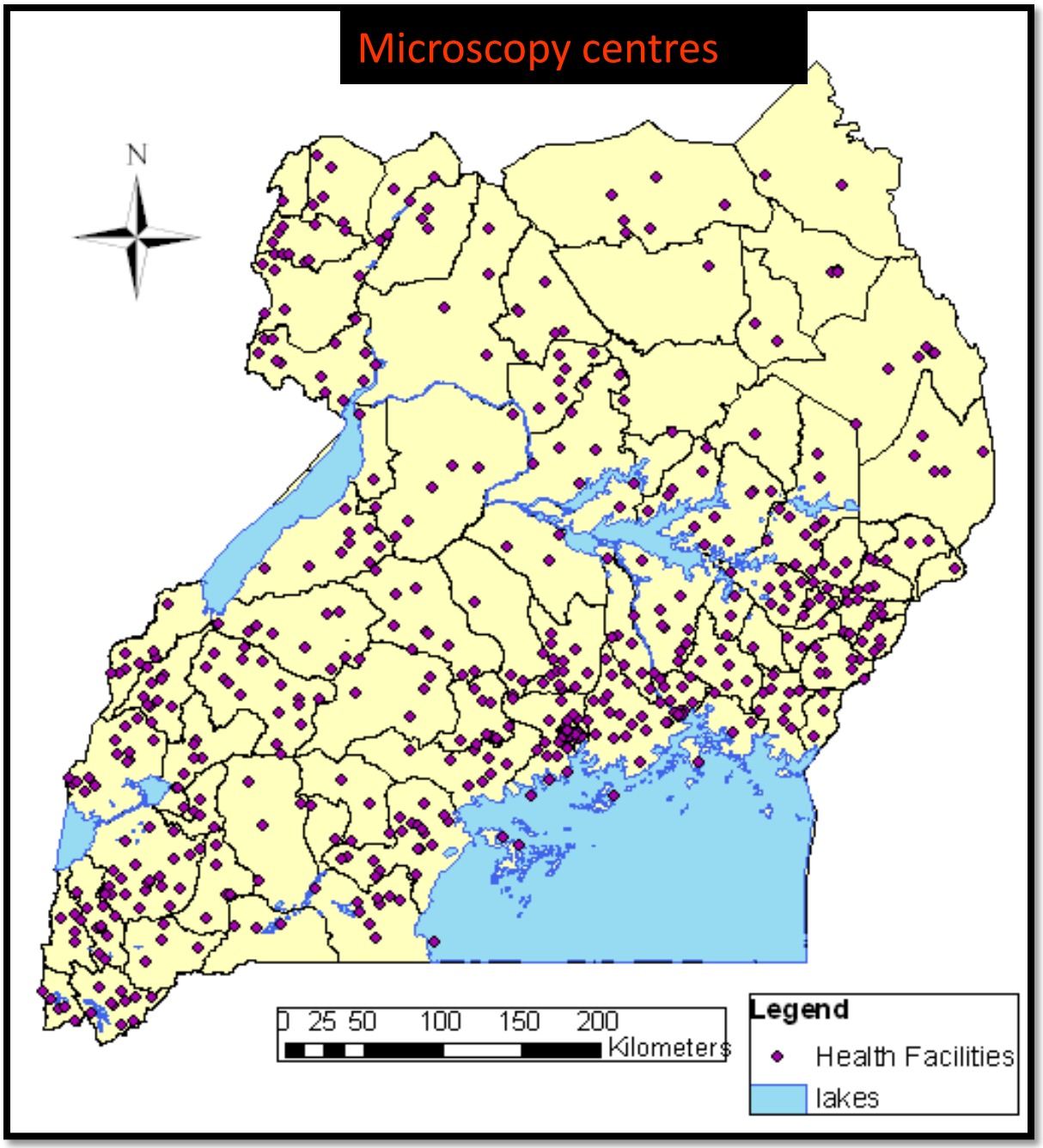
Over view of lab set up

UGANDA TB LABORATORY NETWORK

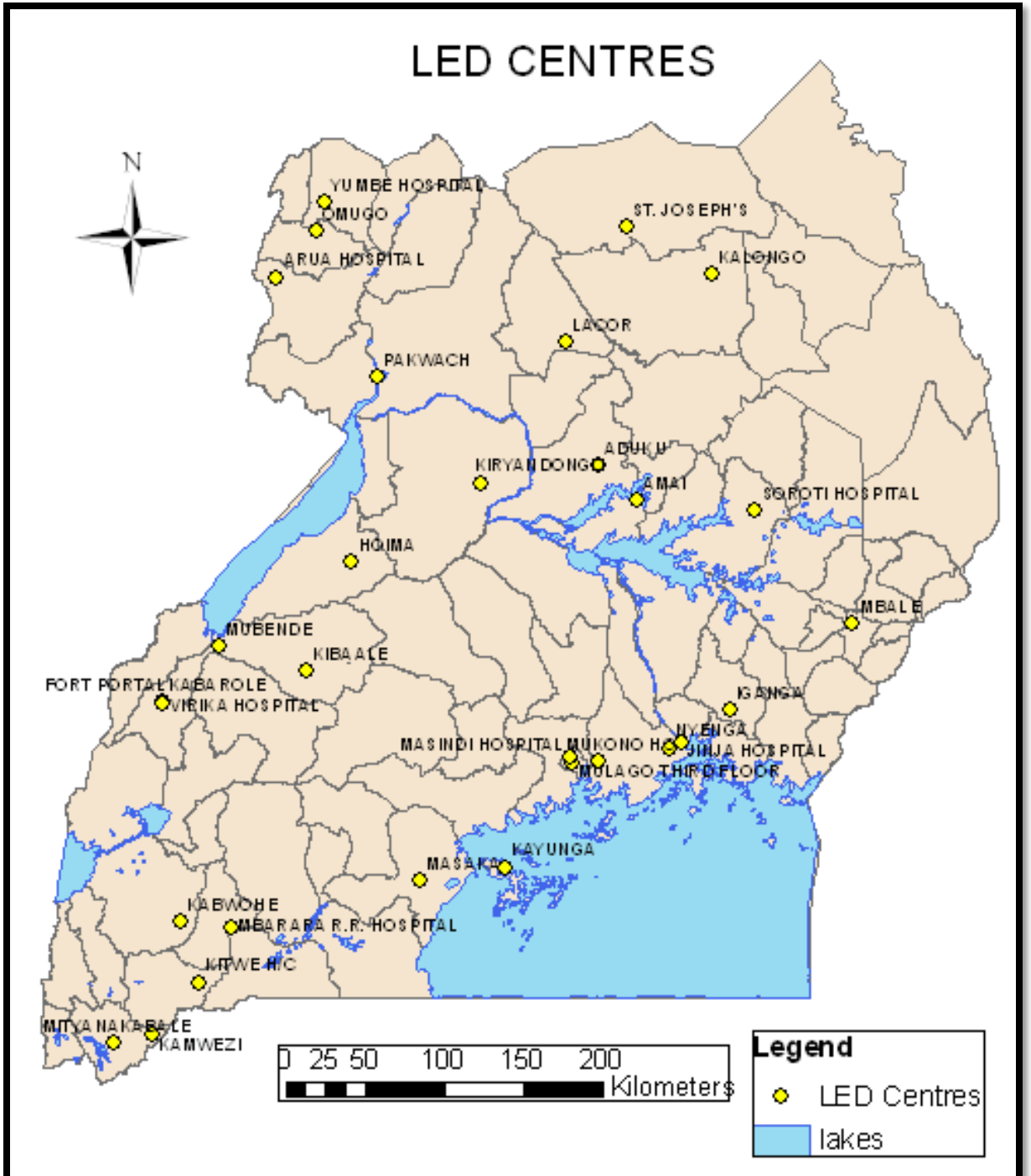


Access to TB diagnostics in Uganda tiered health system





~1000 centres


LED CENTRES
N
YUMBE HOSPITAL
OMUGO
ARUA HOSPITAL
ST. JOSEPH'S
KALONGO
LACOR
PAKWACH
KIRYANDONGO
ADJUKU
AMAI
SOROTI HOSPITAL
HOIMA
MBALE
MUBENDE
KIBAALE
FORT PORTAL
KABAROLE
VIRIKA HOSPITAL
IGANGA
MASINDI HOSPITAL
MUKONO H
NYENGA
JINJA HOSPITAL
MULAGO THIRD FLOOR
KAYUNGA
MASAKA
KABWOHE
MBARARA R.R. HOSPITAL
KITWE H/C
MITYANA
KABALE
KAMWEZI
0 25 50 100 150 200
Kilometers
Legend
LED Centres
lakes

100 LEDs

Problem:

1. Centralized testing
2. Slow diagnostics

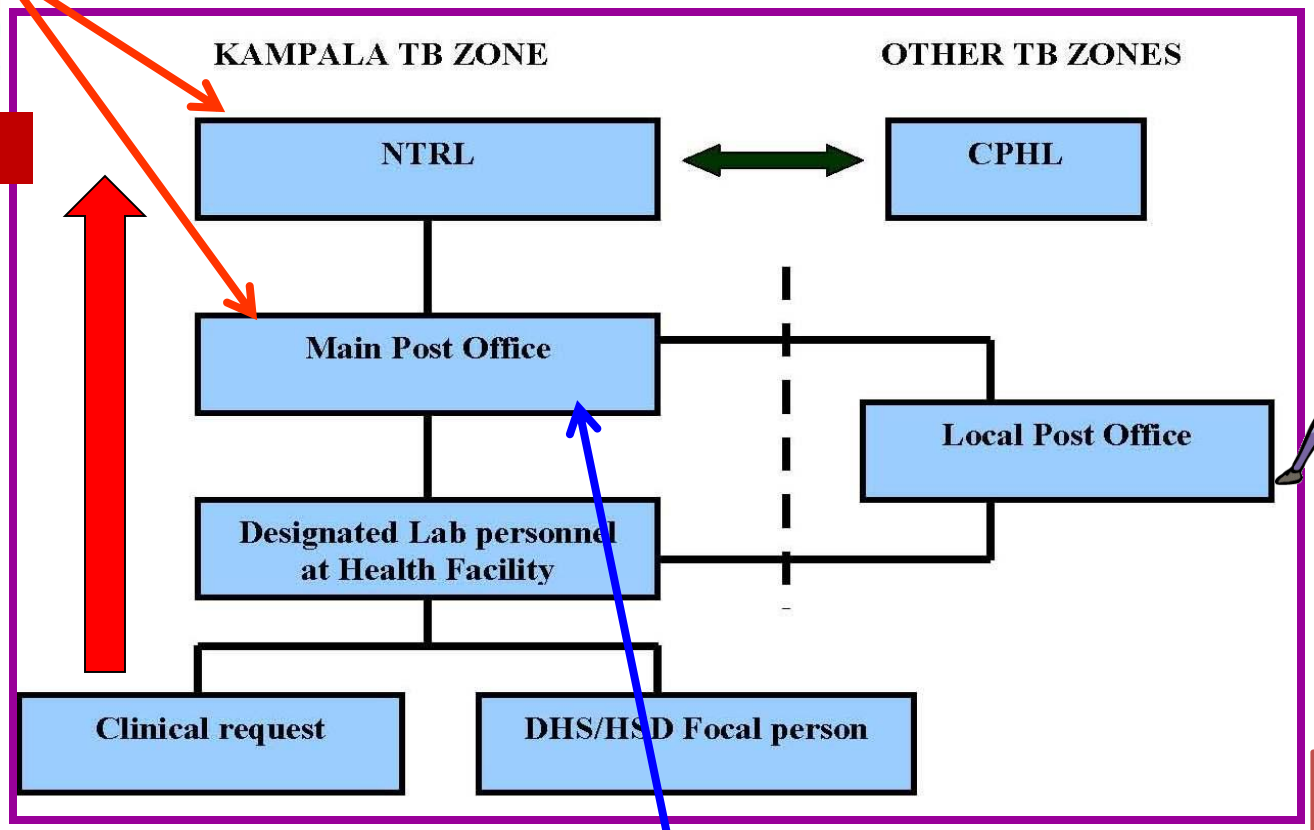
Solution – phase I

- Improve sample referral & result dispatch
- Improve diagnostics - rapid

Rapid sample transportation and result dispatch is key

Toll free line

Samples



LIS –

COMPUTER SOLUTIONS

Results sent electronically

Partnering with Post Office, member of Stop TB

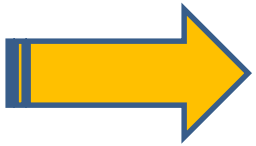
Improved Drug susceptibility testing (DST)

Indirect proportion

by LJ and Bactec 460

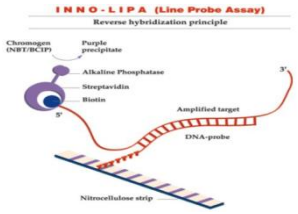
Genotype MTBDR – Rapidly Detects MDR TB

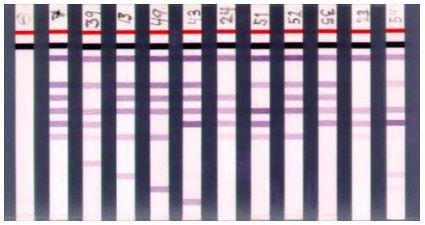
TAT 3 month



PCR Detection

Hybridization

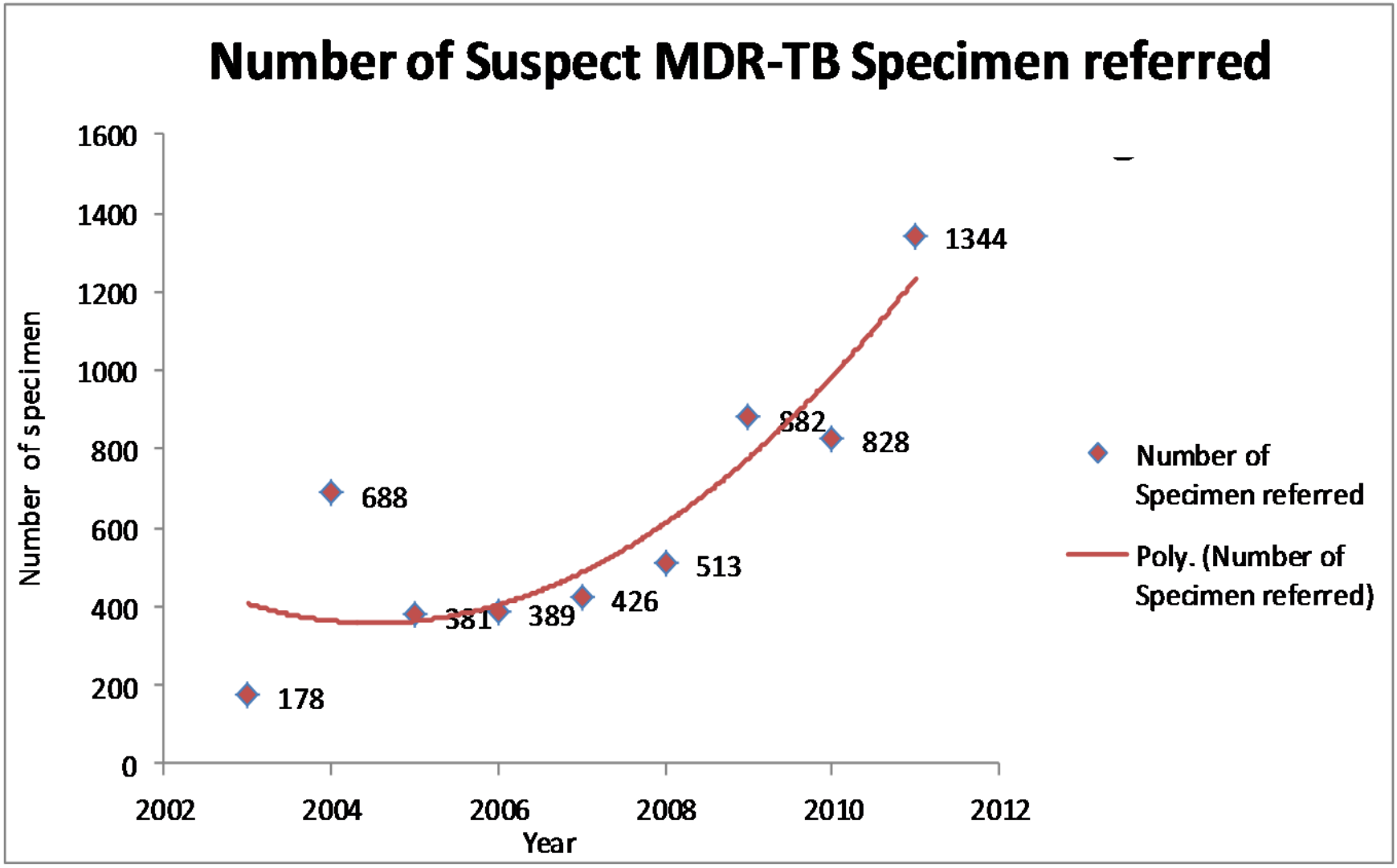




TAT 3 weeks

TAT 2 days

Results – phase 1


Number of Suspect MDR-TB Specimen referred
1600
1400
1200
1000
800
600
400
200
0
Number of specimen
2002
2004
2006
2008
2010
2012
Year
178
688
381
389
426
513
882
828
1344
Number of Specimen referred
Poly. (Number of Specimen referred)

NO.OF DAYS BETWEEN COLLECTION AND RECEIPT OF SAMPLES

Jan - Dec 2008

Days	Frequency	Cum Percent
0	8	1.2
1	8	2.4
2	19	5.3
3	**23**	**8.9**
4	23	12.4
5	32	17.3
6	55	25.6
7	37	31.3
8	42	37.7
9	41	44.0
10	31	48.7
11	21	51.9
12- 239	315	100.0
Total	**655**	**100**

Baseline:

Start of referral system

8.9% in 3 days: Avg 17 days

NO.OF DAYS BETWEEN COLLECTION AND RECEIPT OF SAMPLES

Jan-2011-Dec 2011

	No .of samples	Percent	Cumulative Percent
0	4128	71.0	71.0
1	846	14.6	85.6
2	301	5.2	90.7
3	201	3.5	94.2
4	101	1.7	95.9
5	45	.8	96.7
6	48	.8	97.5
7	48	.8	98.4
8	24	.4	98.8
9	15	.3	99.0
10 - 19	56	.8	100.0
Total	**5813**	**100.0**	

94.2% of samples came within the set TAT of 3 days: Avg 2 days

Time from Collection to Receipt at NTRL (All samples, Jan - Dec 2012)

Days	Freq	Cum %
0	4617	49.7
1	2695	78.7
2	749	86.7
3	538	92.5
4	247	95.2
5	154	96.8
6	85	97.7
7 - 27	211	100.0
Total	**9296**	

Time from Collection to Receipt at NTRL (Outside Kampala, Jan - Dec 2012)

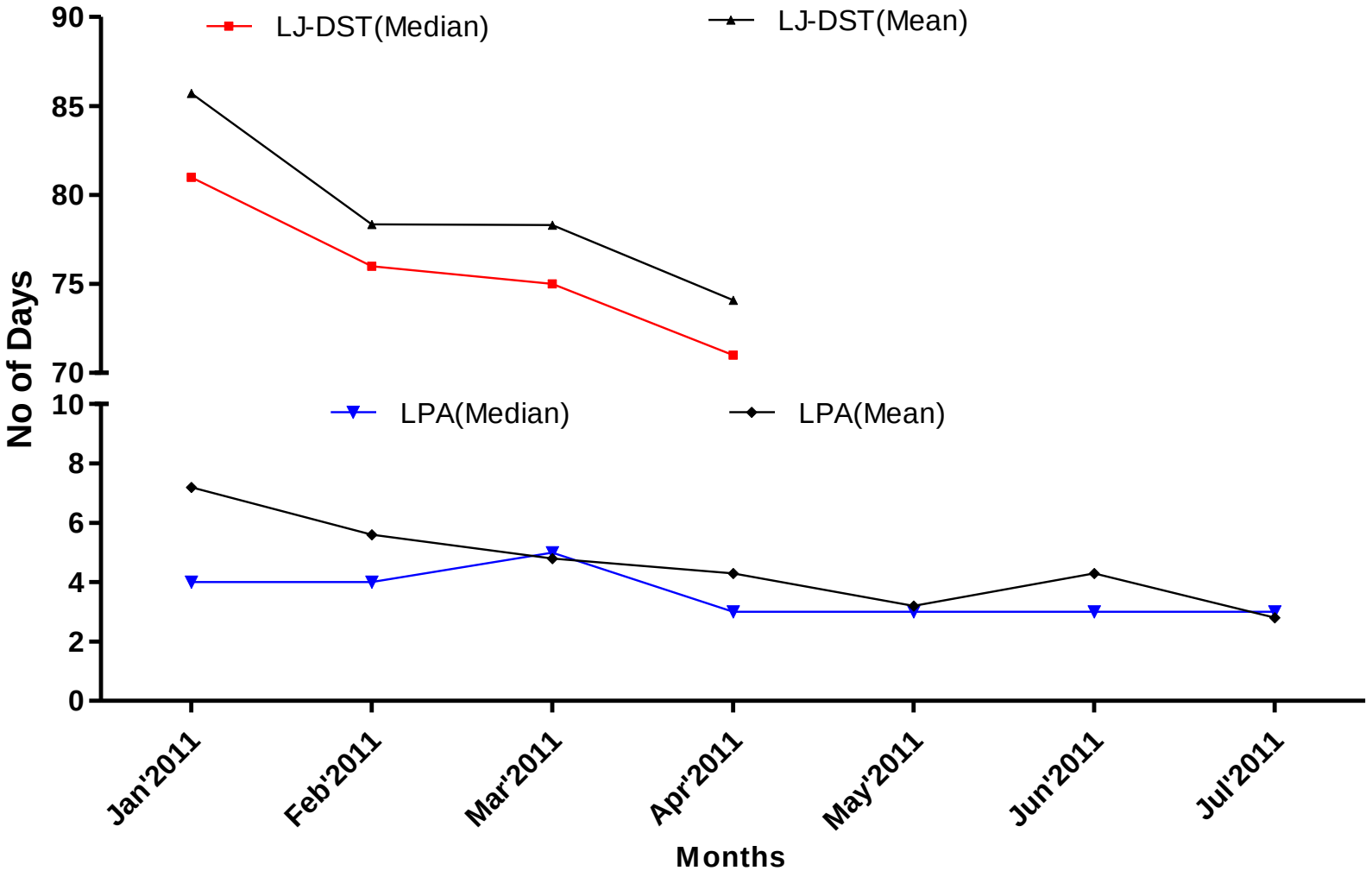
Days	Freq	Cum %
0	712	31.9
1	425	50.9
2	584	77.0
3	172	84.7
5	110	89.7
6	79	93.2
7	55	95.7
8 - 26	97	100.0
Total	**2234**	

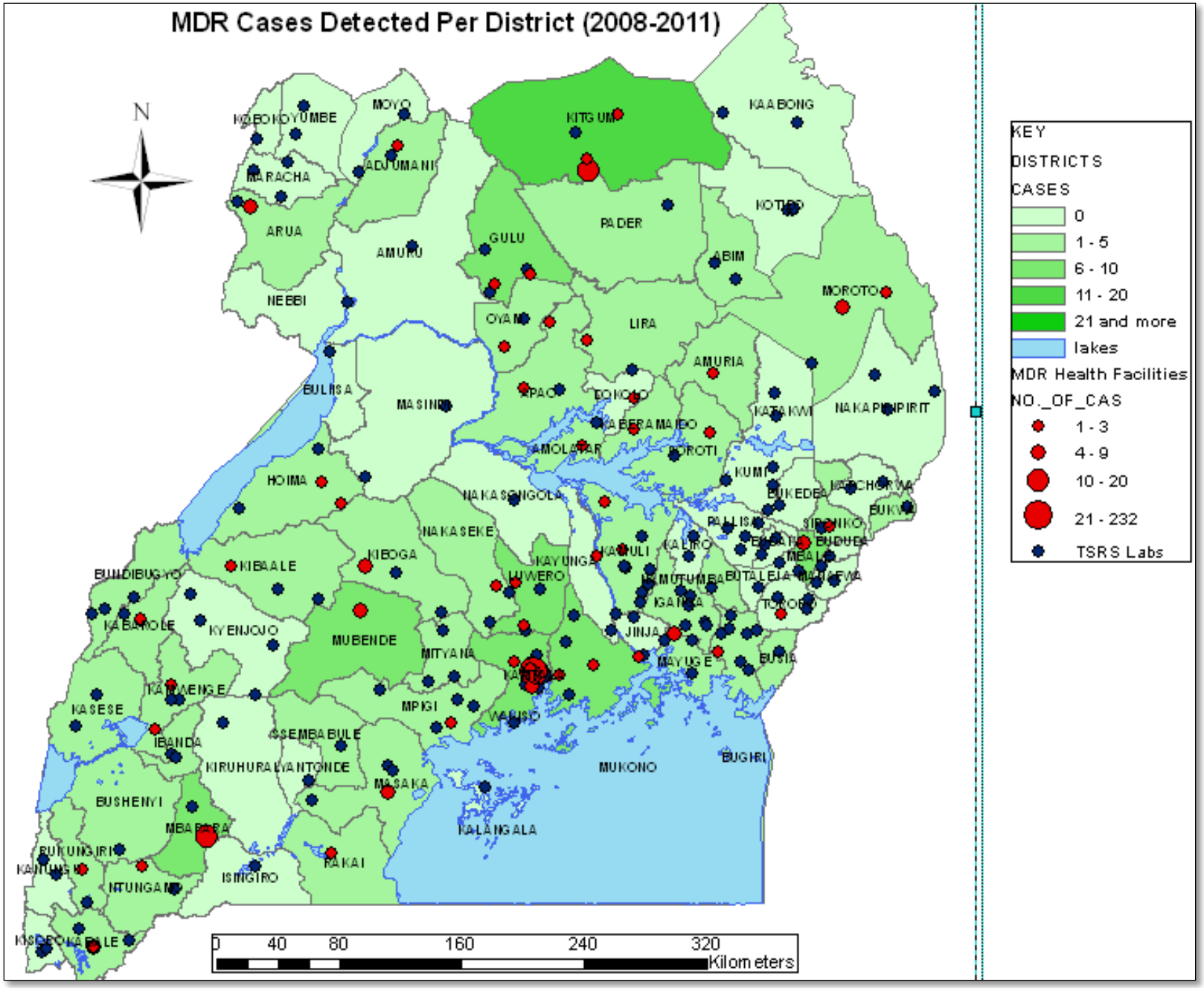
Jan - Dec 2013

	Days	Freq	Cum %
	0-3	7581	83.6
	4-7	1194	96.8
	>7	290	100.0
	Total	**9065**	

- 70% of results are dispatched electronically

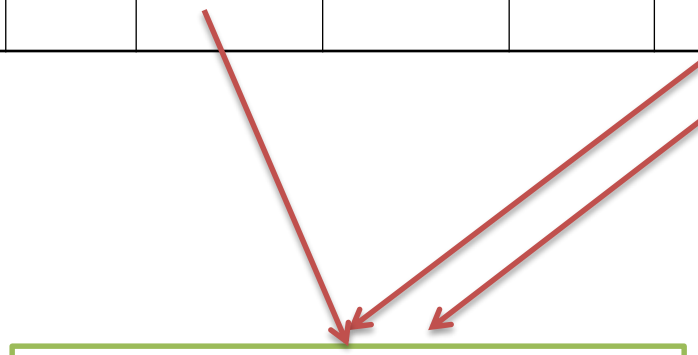
LPA/LJ-DST TAT FROM RECEPTION TO DISPATCH FOR 2011




MDR Cases Detected Per District (2008-2011)
N
KEY
DISTRICTS
CASES
0
1 - 5
6 - 10
11 - 20
21 and more
lakes
MDR Health Facilities
NO._OF_CAS
1 - 3
4 - 9
10 - 20
21 - 232
TSRS Labs
KITGUM
KAABONG
KOTIDO
PADER
ABIM
MOROTO
GULU
AMURU
NEBBI
ARUA
MOYO
ADJUMANI
MARACHA
KIBOKOYUMBE
OYAM
LIRA
AMURIA
KATAKWI
NAKAPIRIPIRIT
BULISA
MASINDI
APAC
KABERAMAIDO
AMOLATAR
SOROTI
KUMI
BUKEDEA
HOIMA
NAKASONGOLA
NAKASEKE
KIBOGA
KIBAALE
BUNDIBUGYO
KABAROLE
KYENJOJO
MUBENDE
MITYANA
LUWERO
KAYUNGA
KAMULI
KALIRO
PALLISA
BUDUDA
BUTALEJA
MBALE
IGANGA
JINJA
MAYUGE
BUSIA
TORORO
TAMWENGE
KASESE
MPIGI
WAKISO
IBANDA
SSEMBABULE
KIRUHURA
LYANTONDE
MASAKA
MUKONO
BUGIRI
BUSHENYI
MBARARA
KALANGALA
BUKUNGIRI
KANUNGU
ISINGIRO
RAKAI
NTUNGAMO
KISORO
KABALE
0 40 80 160 240 320
Kilometers

Proportion of previously treated patients tested - 2011

PTB											Total
New M +	CDR %	New M -	NSD N	Relapse +	Relapse -	NSD R	Def +	Fail +	Other	EPTB	
25,614	57.2%	12,830	1,559	1,302	534	107	1,206	306	559	5,001	49,018



1344 / 2814 = 48%

Solution – Phase II

1. Expand & integrate referral system
   – HUB system

2. Decentralize testing

Collection HUBs to improve access to the peripheral centers

Boda boda to aid sample and result delivery

PL

Integrated sample referral

PL

HUB

PL

Rif resistant TB samples

Post office

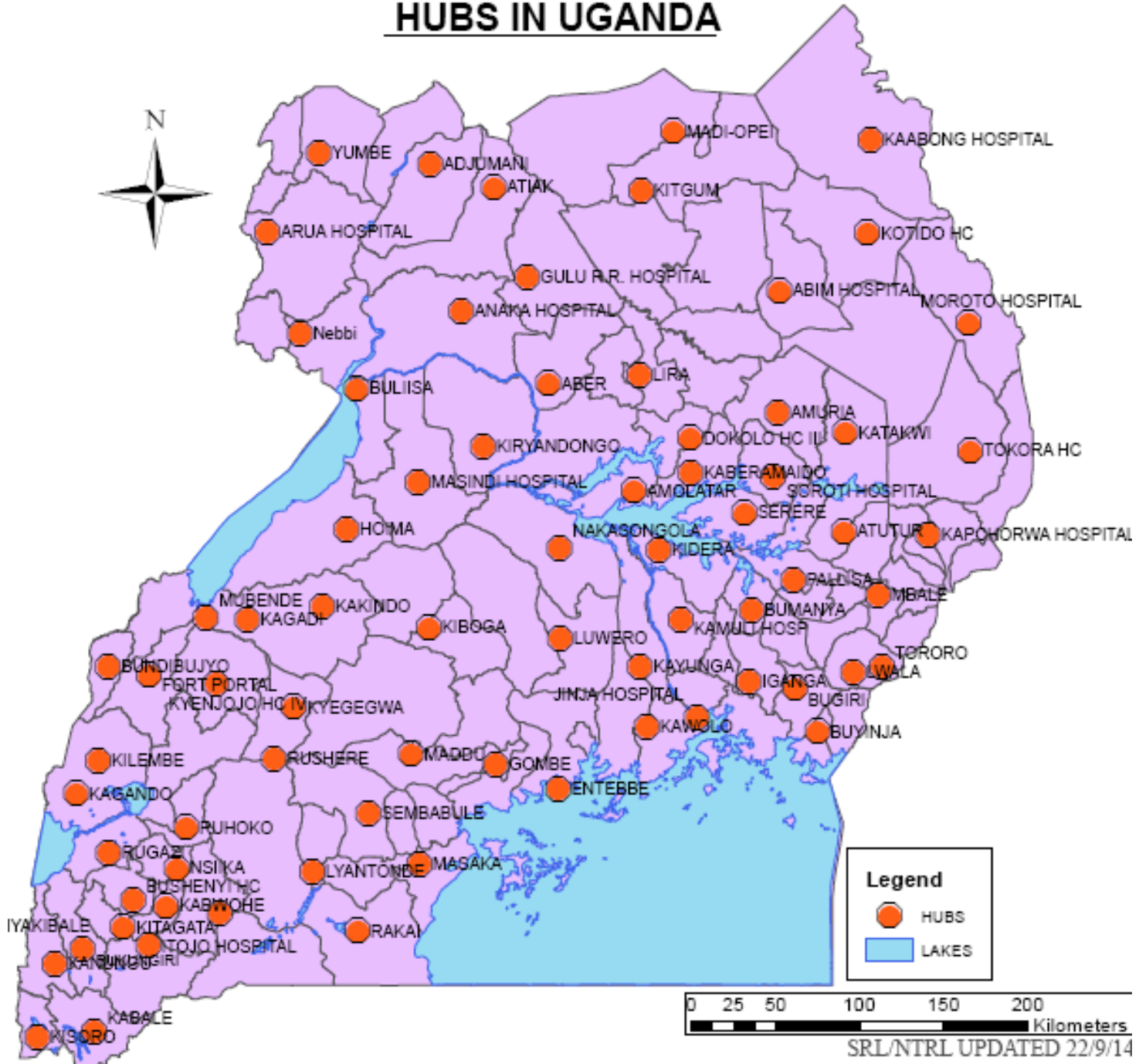
NTRL

LPA/culture

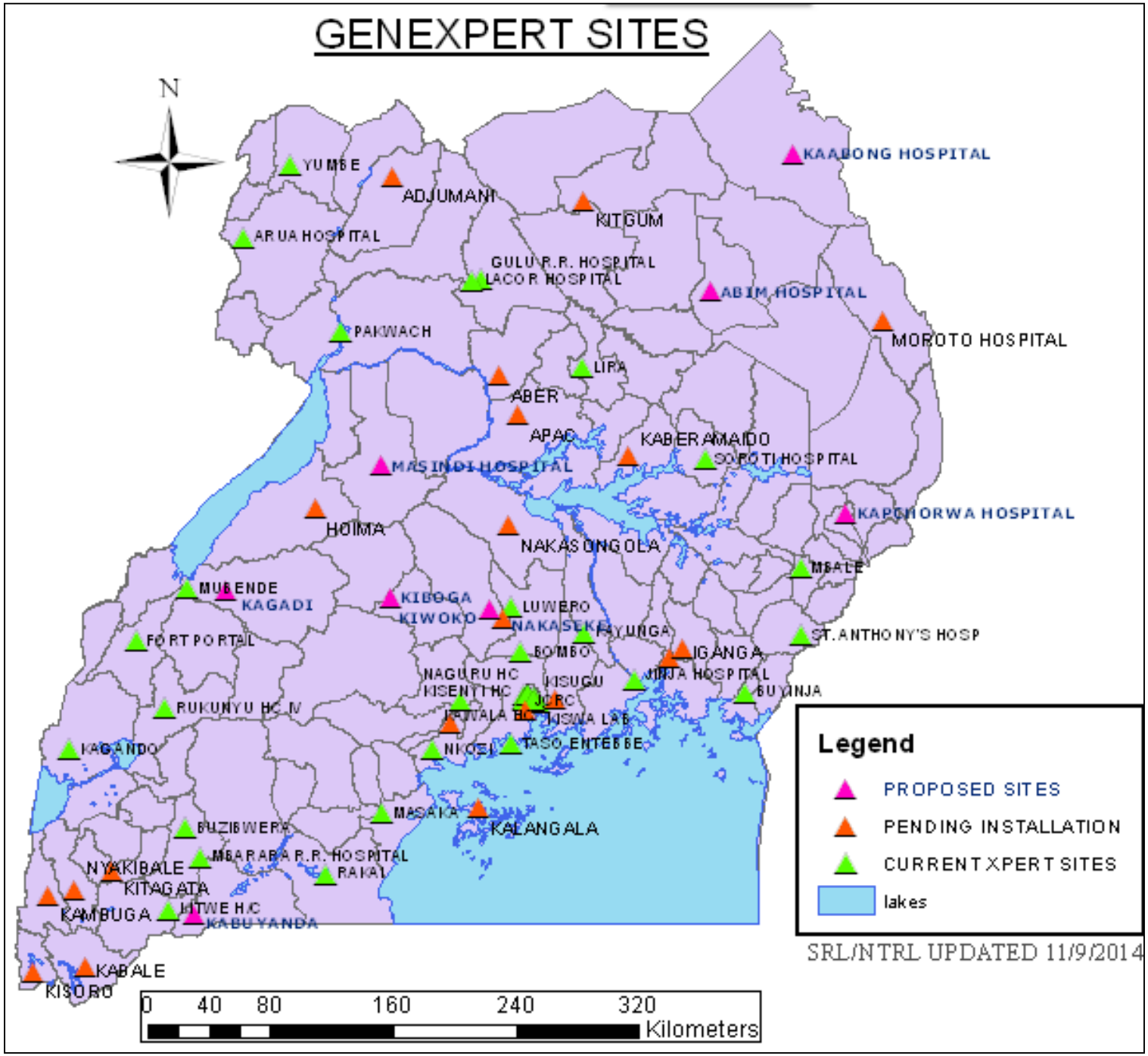
PL

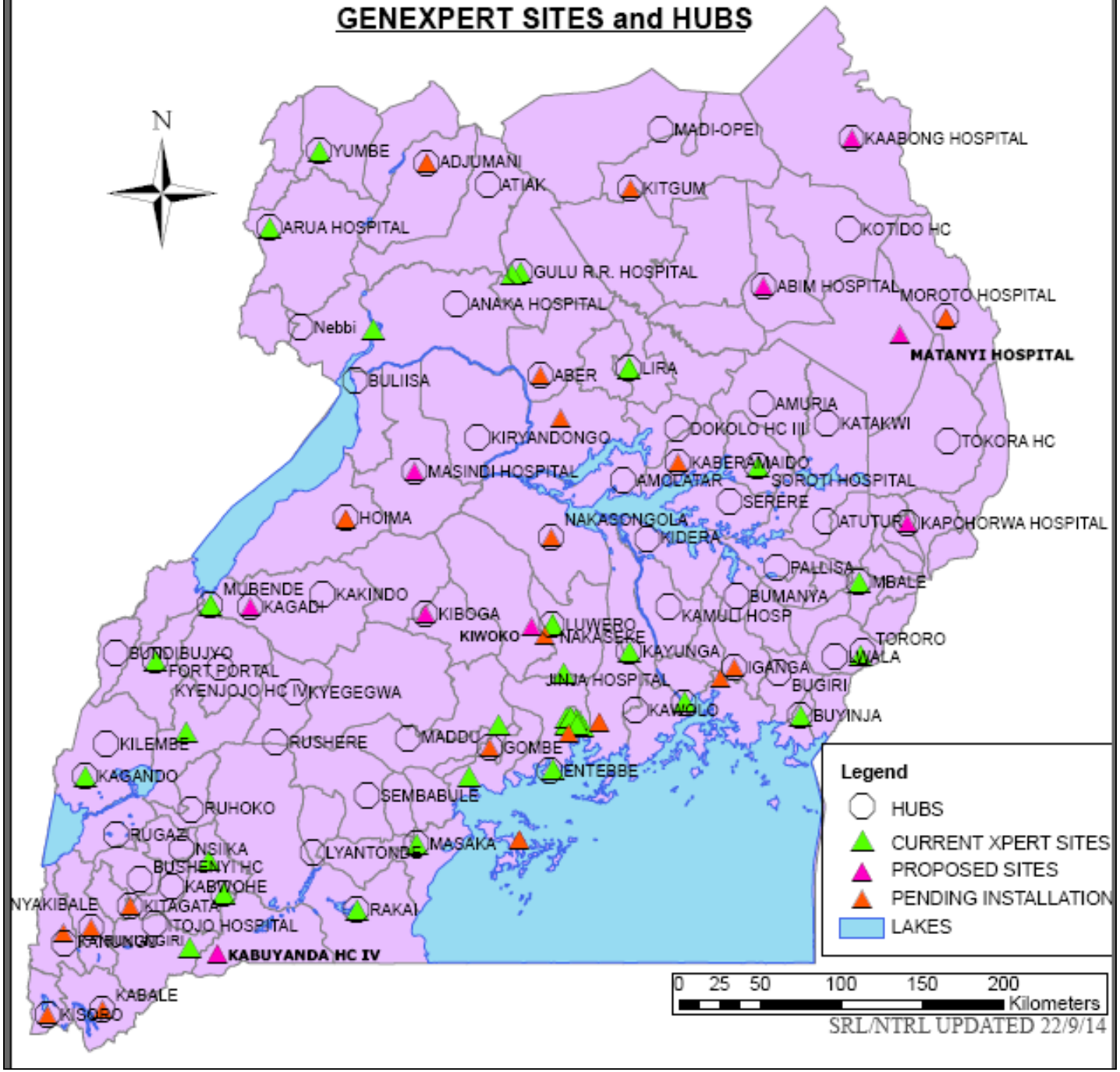
Toll free line

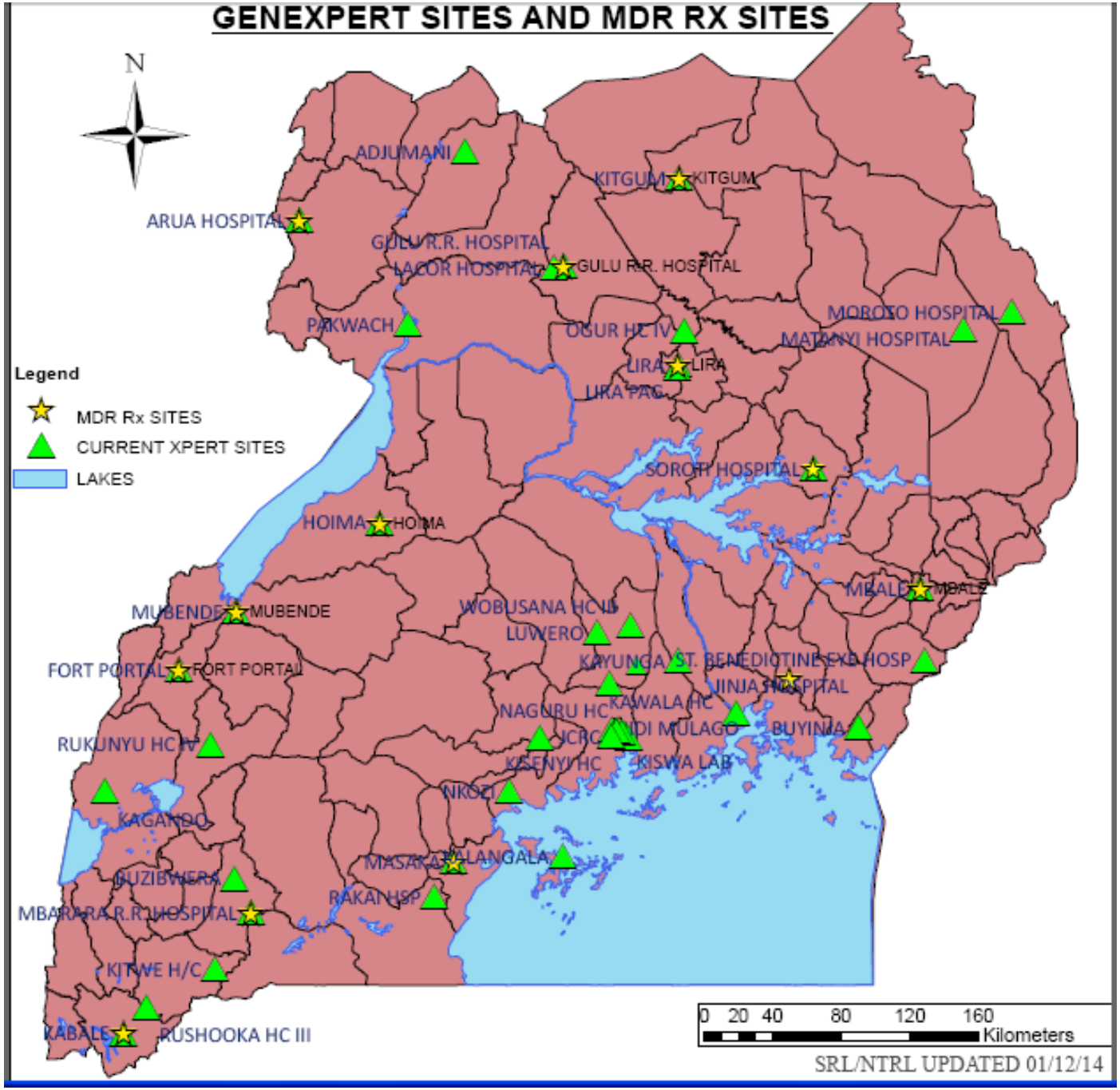
HUBS IN UGANDA



SRL/NTRL UPDATED 22/9/14

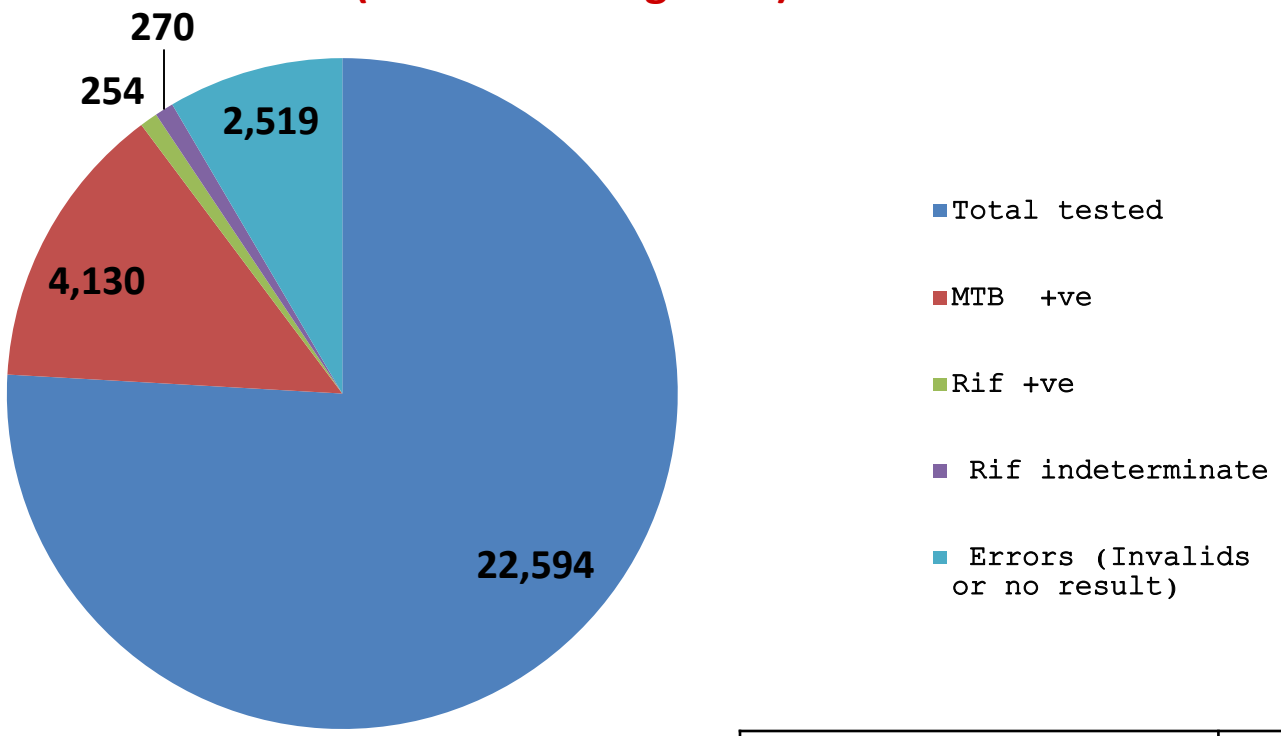

GENEXPERT SITES
N
YUMBE
ADJUMANI
KITGUM
KAABONG HOSPITAL
ARUA HOSPITAL
GULU R.R. HOSPITAL
LACOR HOSPITAL
ABIM HOSPITAL
MOROTO HOSPITAL
PAKWACH
LIRA
ABER
APAC
KABERAMAIDO
SOROTI HOSPITAL
MASINDI HOSPITAL
KAPCHORWA HOSPITAL
HOIMA
NAKASONGOLA
MBALE
MUBENDE
KAGADI
KIBOGA
KIWOKO
LUWERO
NAKASEKE
MUKONO
ST.ANTHONY'S HOSP
FORT PORTAL
BOMBO
IGANGA
NAGURU HC
KISENYI HC
KISUGU
JCRC
MINJA HOSPITAL
BUYINJA
RUKUNYU HC IV
KAGANDO
TASO ENTEBBE
MASAKA
KALANGALA
BUZIBWERA
MBARARA R.R. HOSPITAL
RAKAI
NYAKIBALE
KITAGATA
KAMBUGA
KITWE HC
KABUYANDA
KABALE
KISORO
Legend
PROPOSED SITES
PENDING INSTALLATION
CURRENT XPERT SITES
lakes
SRL/NTRL UPDATED 11/9/2014
0 40 80 160 240 320
Kilometers


GENEXPERT SITES and HUBS
N
YUMBE
ADJUMANI
ATIAK
MADI-OPEI
KAABONG HOSPITAL
KITGUM
ARUA HOSPITAL
KOTIDO HC
GULU R.R. HOSPITAL
ABIM HOSPITAL
MOROTO HOSPITAL
ANAKA HOSPITAL
Nebbi
MATANYI HOSPITAL
BULIISA
ABER
LIRA
AMURIA
KATAKWI
KIRYANDONGO
DOKOLO HC III
TOKORA HC
KABERAMAIDO
MASINDI HOSPITAL
AMOLATAR
SOROTI HOSPITAL
SERERE
HOIMA
NAKASONGOLA
ATUTUR
KAPCHORWA HOSPITAL
KIDERA
PALLISA
MBALE
MUBENDE
KAGADI
KAKINDO
BUMANYA
KIBOGA
KAMULI HOSP
LUWERO
KIWOKO
NAKASERE
TORORO
BUNDIBUJYO
KAYUNGA
LWALA
FORT PORTAL
IGANGA
KYENJOJO HC IV
KYEGEGWA
JINJA HOSPITAL
BUGIRI
KAWOLO
BUYINJA
KILEMBE
RUSHERE
MADDU
GOMBE
KAGANDO
ENTEBBE
SEMBABULE
RUHOKO
RUGAZI
NSIKA
LYANTONDE
MASAKA
BUSHENYI HC
KABWOHE
NYAKIBALE
KITAGATA
RAKAI
TOJO HOSPITAL
KATUNGURI
KABUYANDA HC IV
KABALE
KISORO
Legend
HUBS
CURRENT XPERT SITES
PROPOSED SITES
PENDING INSTALLATION
LAKES
0 25 50 100 150 200
Kilometers
SRL/NTRL UPDATED 22/9/14


GENEXPERT SITES AND MDR RX SITES
N
Legend
MDR Rx SITES
CURRENT XPERT SITES
LAKES
ADJUMANI
KITGUM
KITGUM
ARUA HOSPITAL
GULU R.R. HOSPITAL
LACOR HOSPITAL
GULU R.R. HOSPITAL
MOROTO HOSPITAL
PAKWACH
OGUR HC IV
MATANYI HOSPITAL
LIRA
LIRA
LIRA PAG
SOROTI HOSPITAL
HOIMA
HOIMA
MBALE
MBALE
MUBENDE
MUBENDE
WOBUSANA HC III
LUWERO
KAYUNGA
ST. BENEDICTINE EYE HOSP
FORT PORTAL
FORT PORTAL
JINJA HOSPITAL
KAWALA HC
NAGURU HC
IDI MULAGO
BUYINJA
RUKUNYU HC IV
KISENYI HC
KISWA LAB
NKOZI
KAGADI
MASAKA
KALANGALA
BUZIBWERA
RAKAI HSP
MBARARA R.R. HOSPITAL
KITWE H/C
KABALE
RUSHOOKA HC III
0 20 40 80 120 160
Kilometers
SRL/NTRL UPDATED 01/12/14

GX Data from 28 of 47 sites

(Jun 2013 – Aug 2014)



60 MDR enrolled on RX in Same period

Smear negative	22,594
MTB +ve	4,130
Rif resistant	254
RIF indeterminate	270
Errors (Invalids or no result)	2,519
Rif resistance rate (%)	6.15
Pos rate (%)	18.8
Error rate (%)	11.5

Solution – Phase III

- Data handling

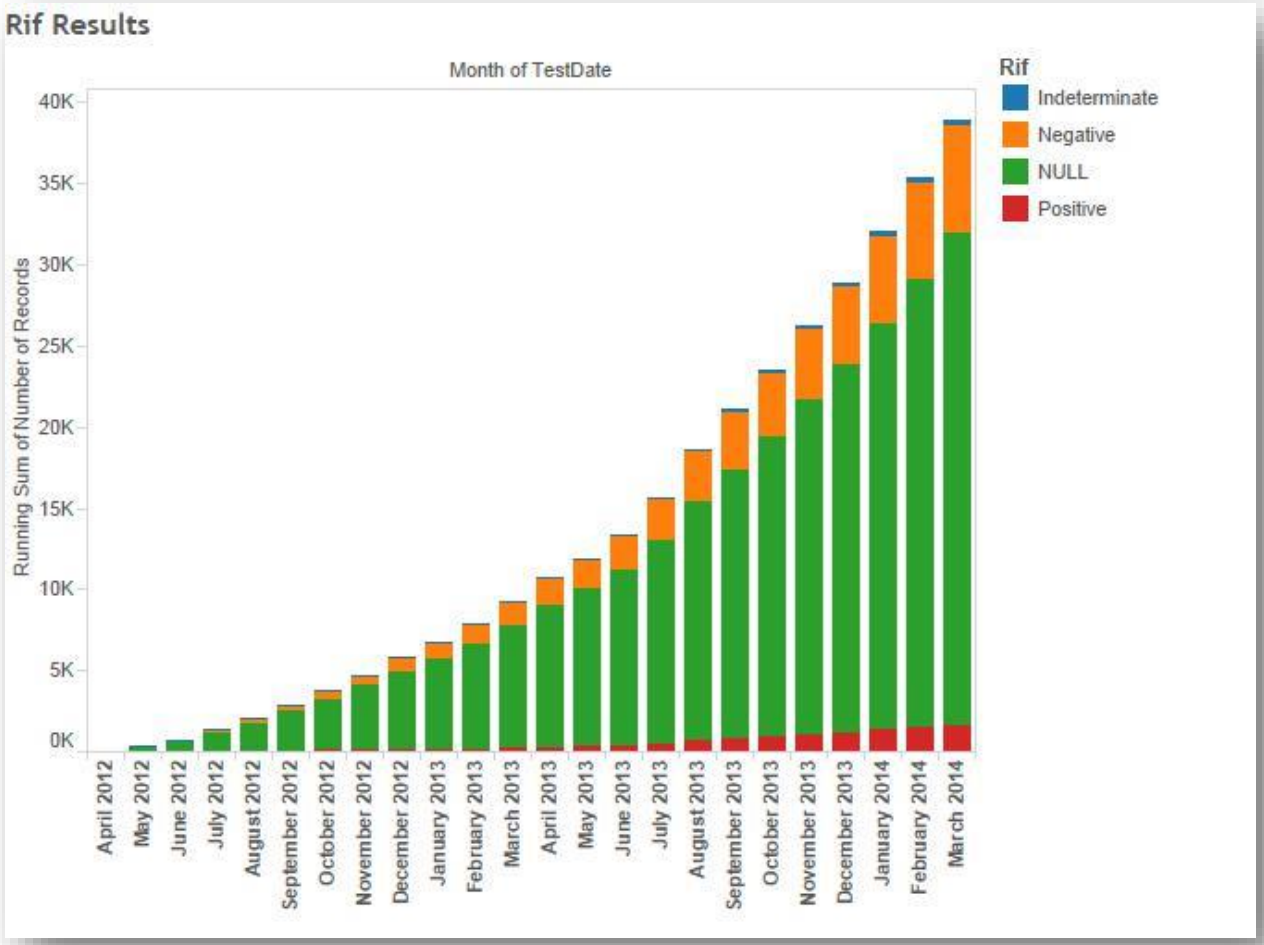
Can we get better quality data, faster?

Does it lead to NTP action?

Do results get to patients?

1

*Can GxAlert get patients into **appropriate treatment faster**?*

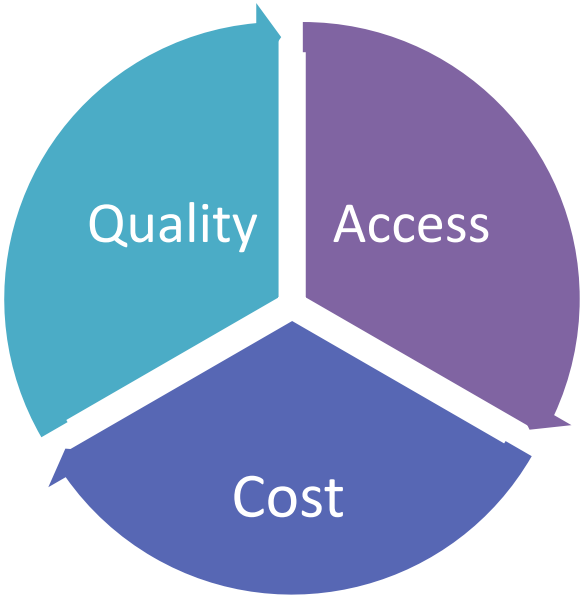


*"We saw **10x** the level of MDR we expected!"*

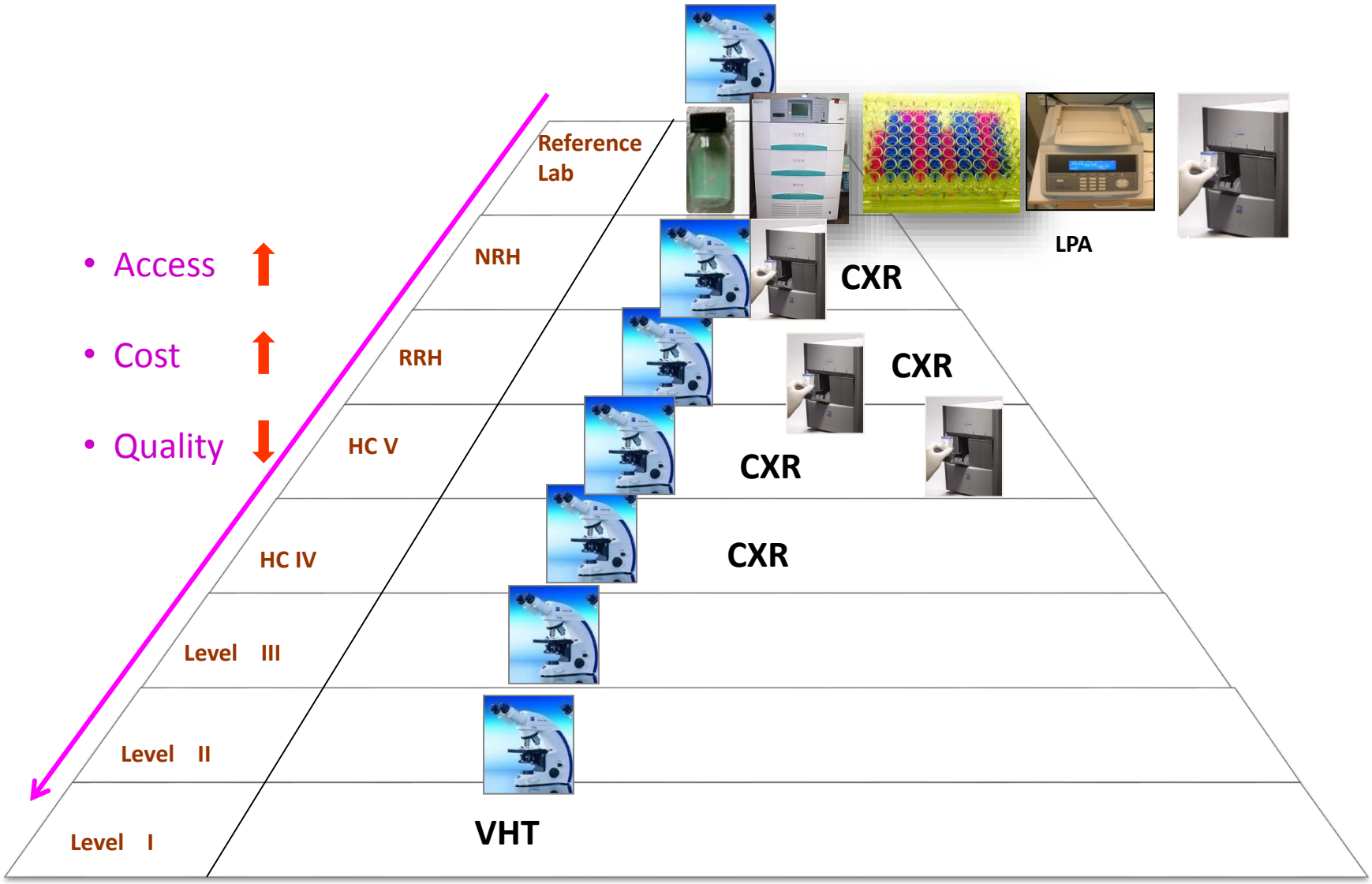
Working on "Clinician Referral"

What is the best surveillance approach?

- **Fast (TAT)** – to allow early initiation of therapy
- **Sensitive** – to detect most of the cases
- **Specific** – to minimize false treatment
- **Accessible** – to have a significant impact
- Cost effective – to be sustainable



As access increases, quality could decrease



Sample referral networks

- Maintain quality
    - At few units
- Improve access

Thank you !!!