Scaling up of viral load testing in rural Zimbabwe: implications for phasing out of d4T

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MSF Zimbabwe Programme
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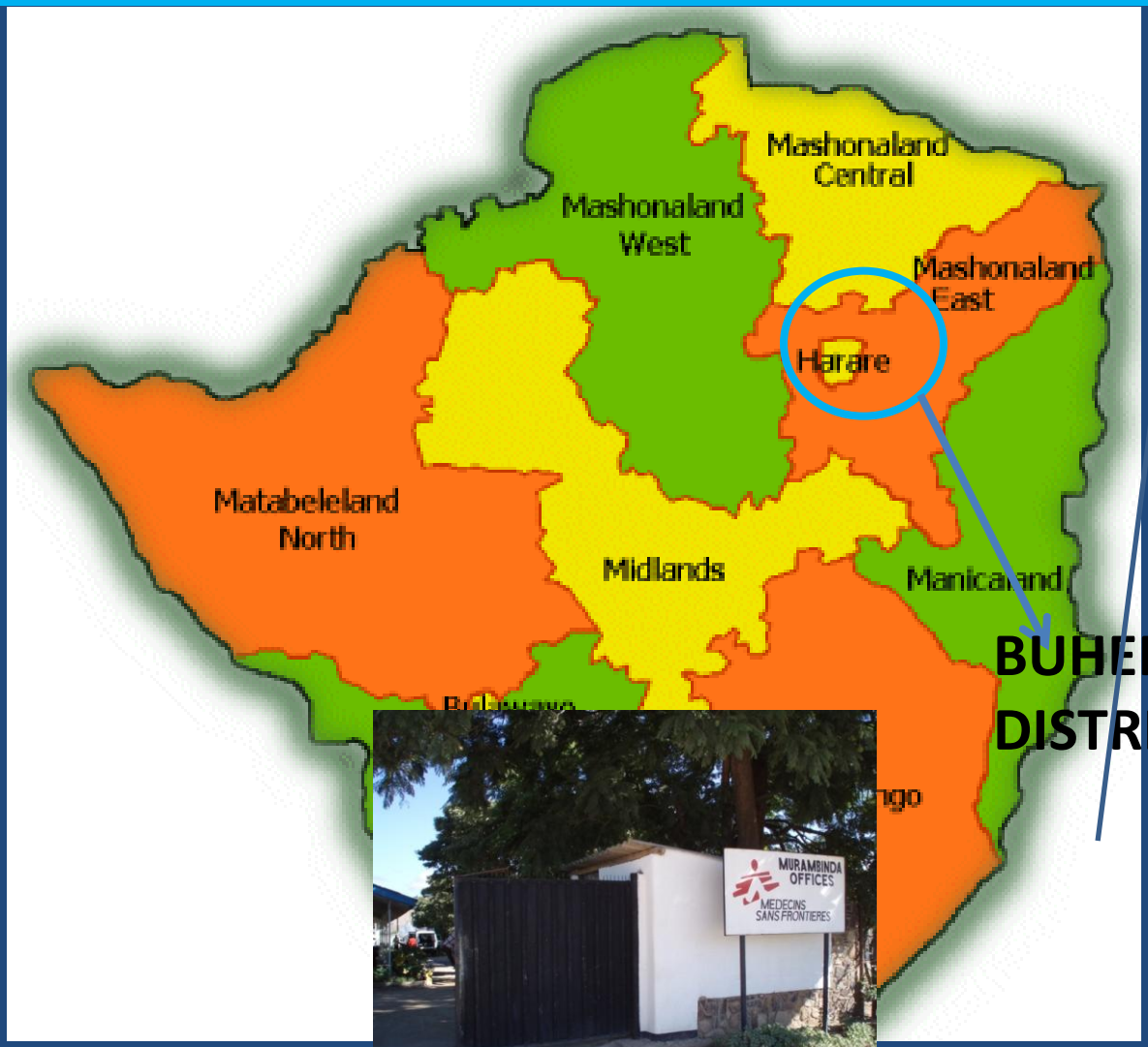
MEDECINS SANS FRONTIERES

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

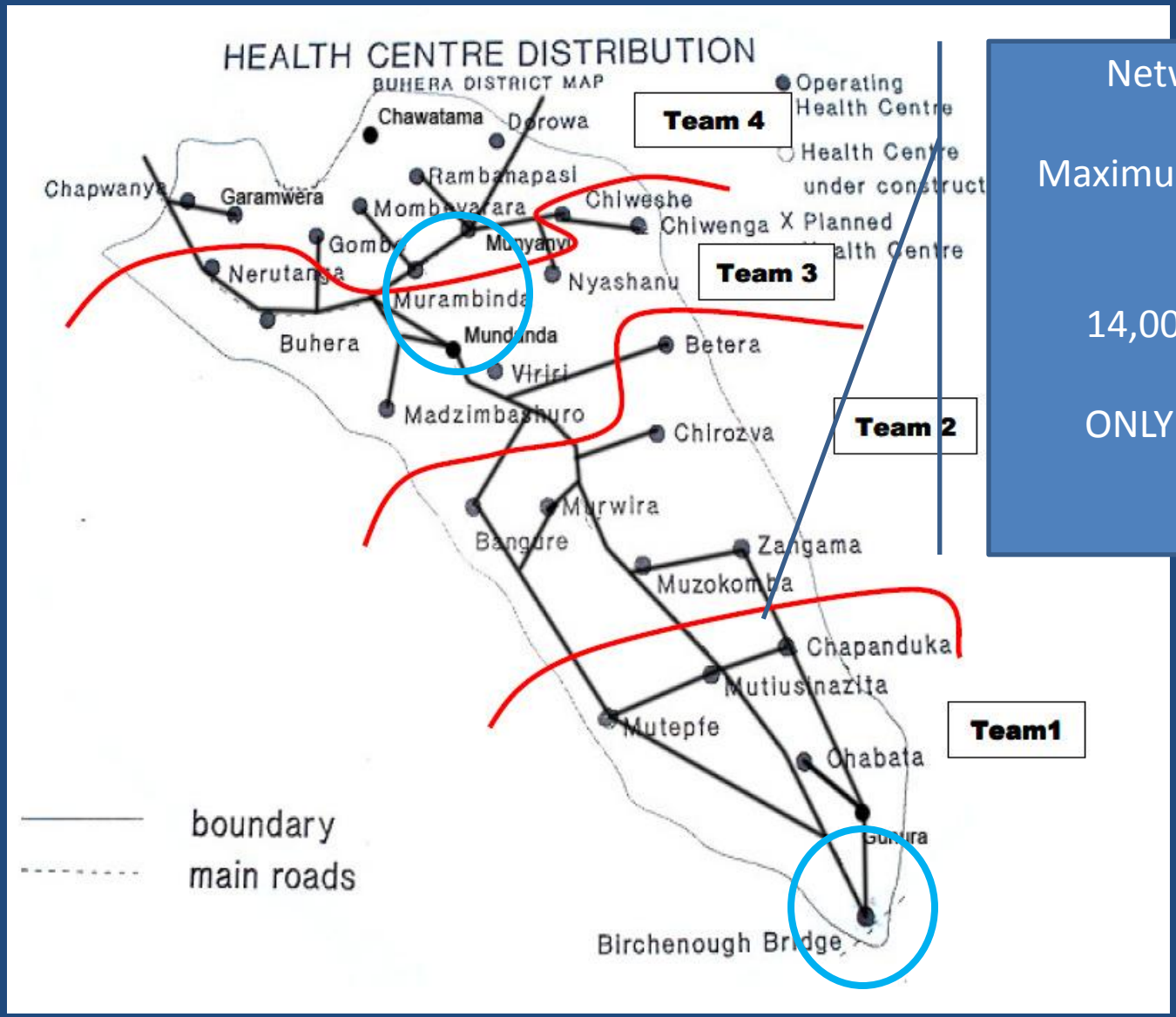
PRIMARY HEALTH CARE • A HEALTHY NATION • MINISTRY OF HEALTH & CHILD WELFARE • ZIMBABWE

1.6%

Background- MSF in Zimbabwe



HIV prevalence
14% in 2009



Network of 25 clinics

Maximum distance to a clinic 70km

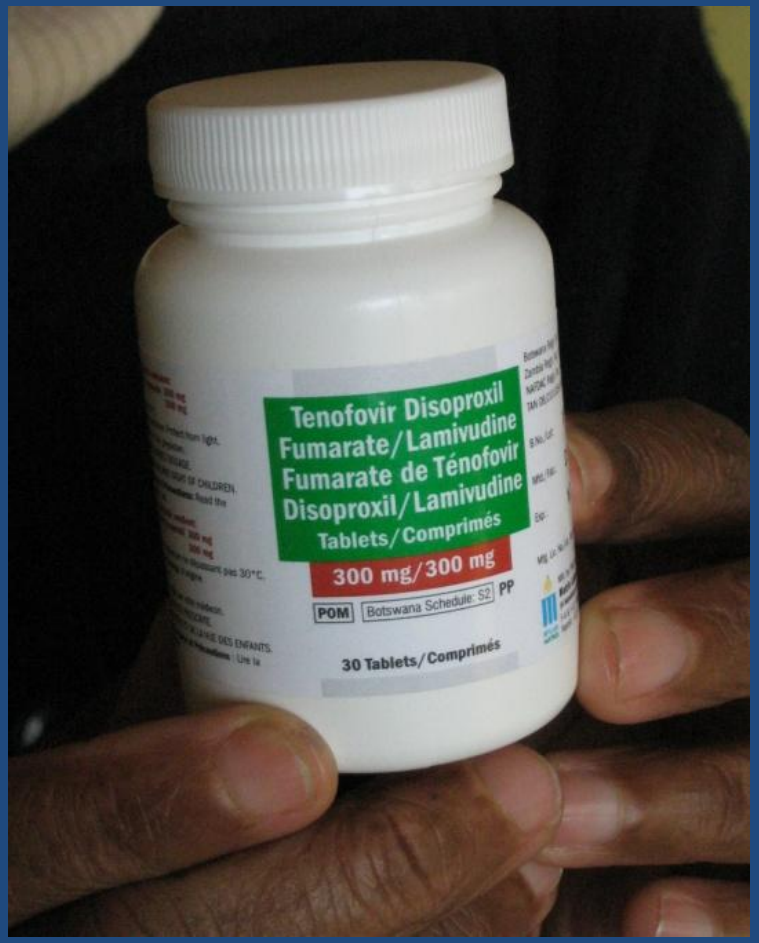
14,000 patients on ART

ONLY 60 on second line

BUHERA DISTRICT- POPULATION 230,000

Introducing A Tenofovir Based First Line

- WHO 2010 guidelines called for phasing out of stavudine and replacing it with the less toxic drug tenofovir (TDF)
- MSF guidelines advised that patients should not be switched without first checking for virological failure



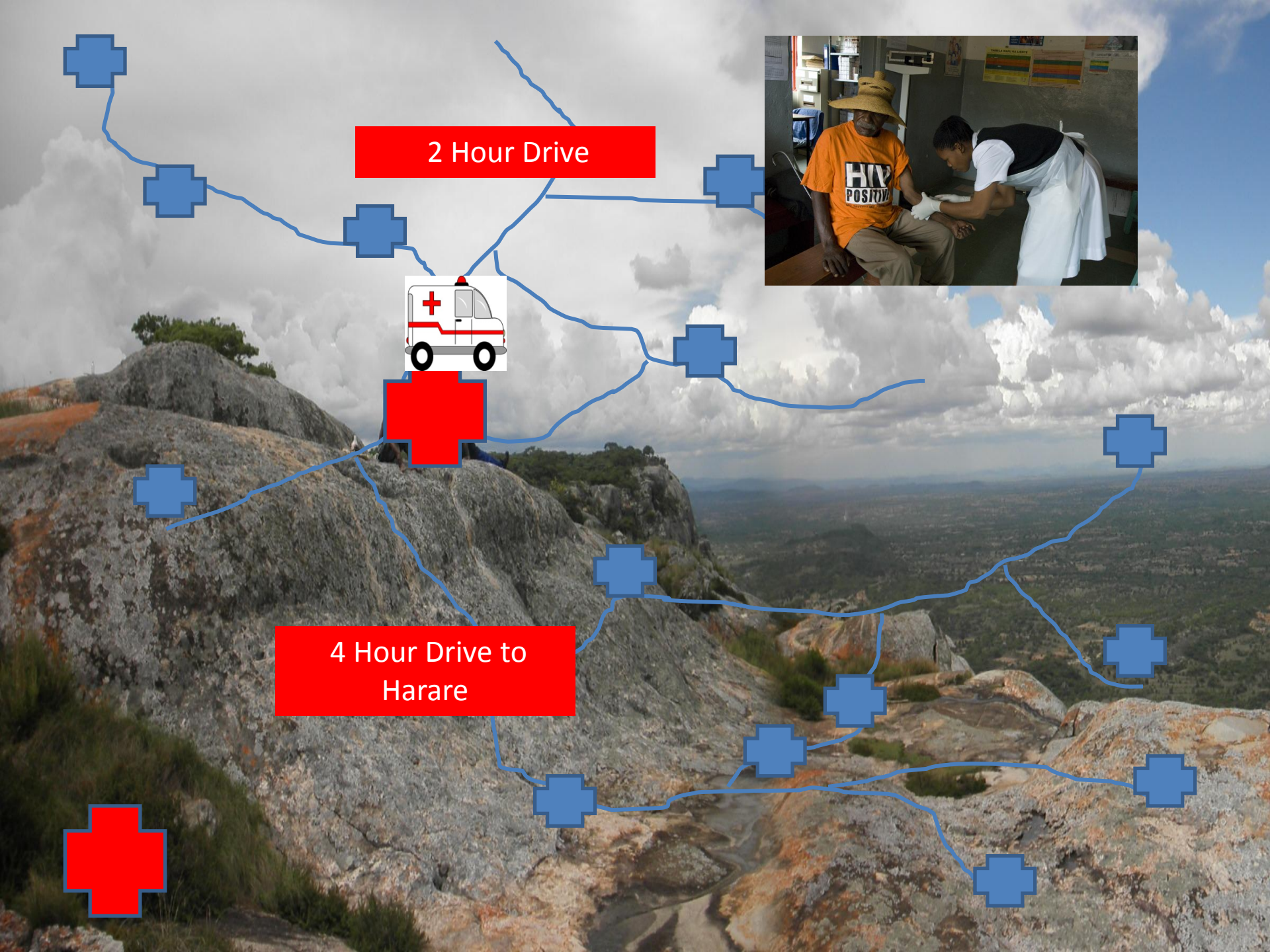
Introducing a Tenofovir Based First Line

- Was this guidance feasible to implement in our programmes?
- How many patients might be failing in a cohort who had never had a viral load before?
- Could we define some risk factors to narrow down who may be at highest risk of failure?

Barriers to rolling out viral load in Zimbabwe

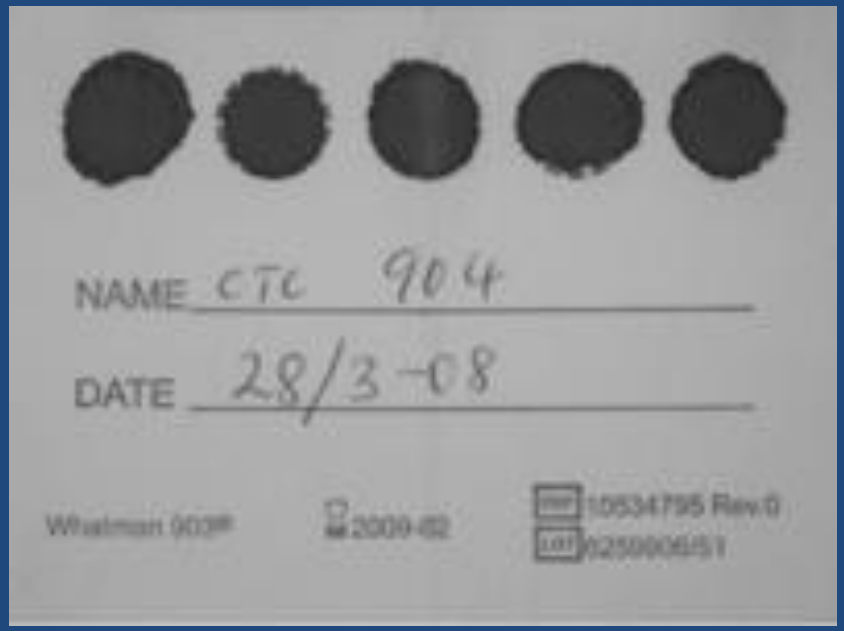
- Technicalities of the test itself- centralised laboratory, qualified lab staff needed
- Sample transport- whole blood needed and on same day (4 hour drive to Harare)
- Need for cold chain
- COST: 90 USD/test + transport costs
- In 2010 only 285 viral loads performe

Overcoming the VL Access barriers
Step 1: Sample transport

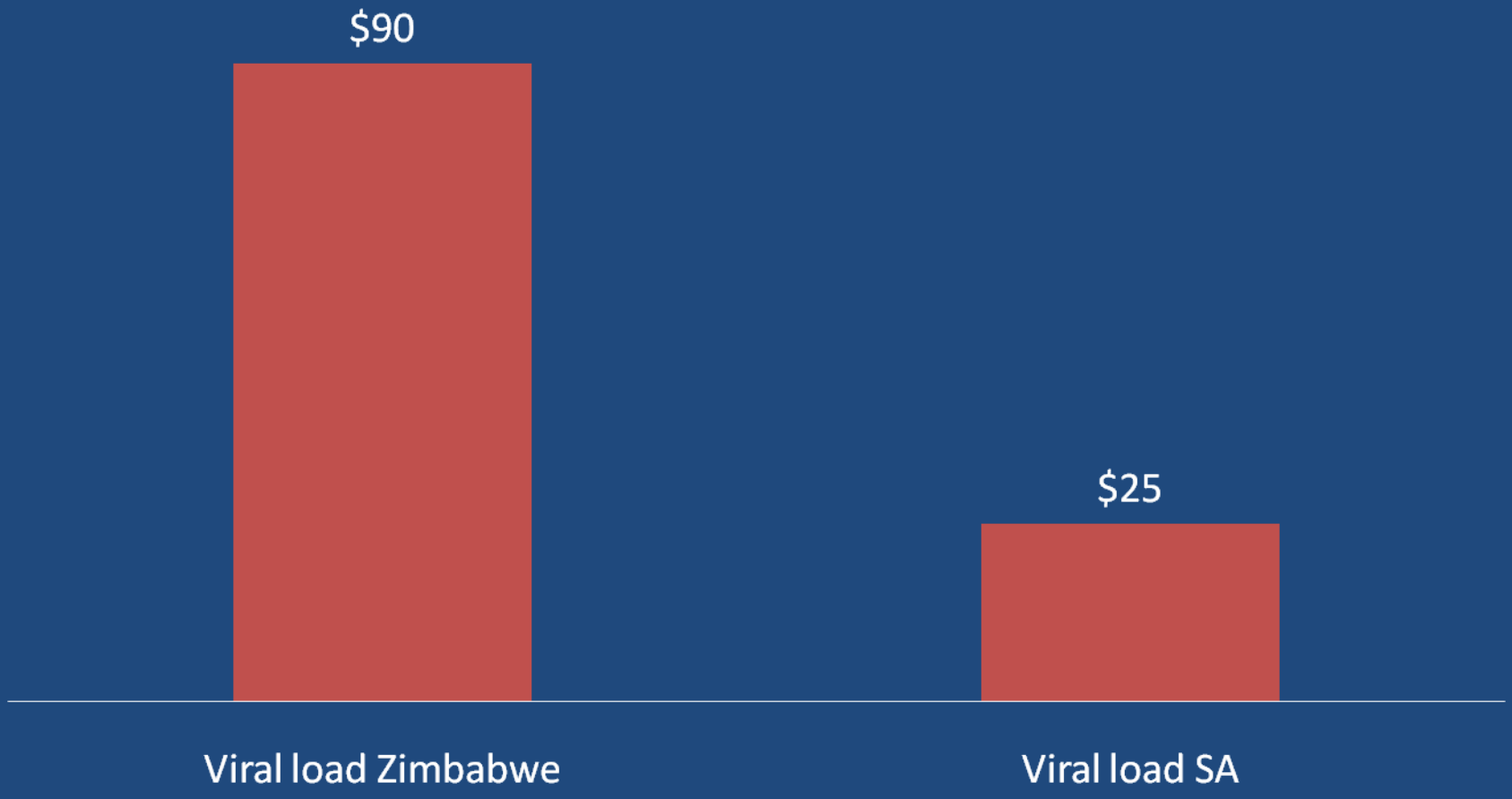

2 Hour Drive
HIV POSITIVE
4 Hour Drive to Harare

Overcoming the VL Access barriers Step 1: Sample transport

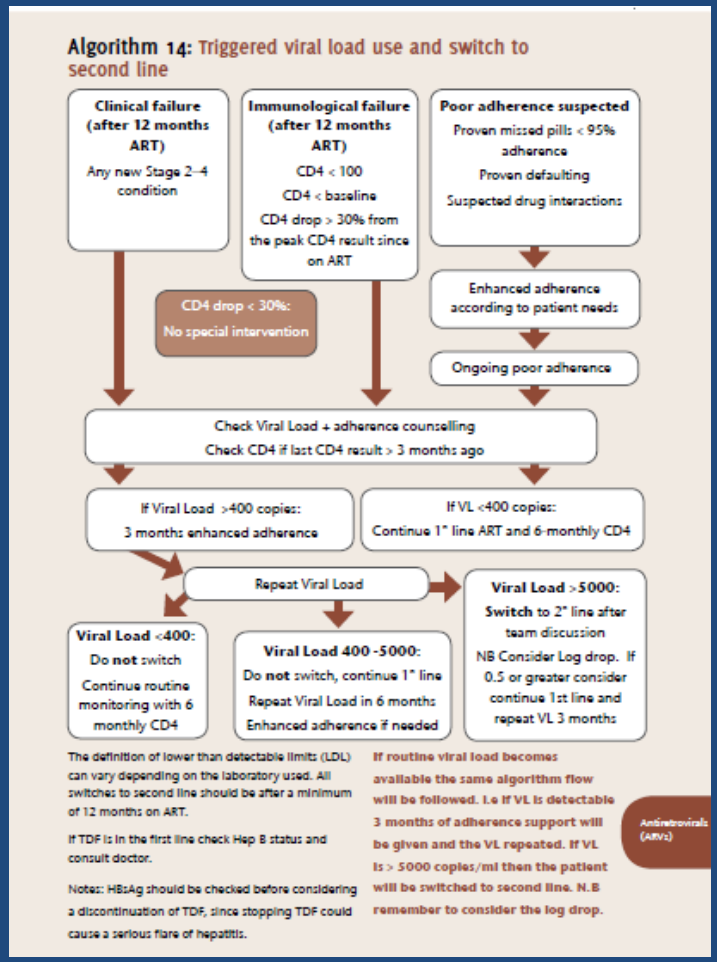
- Introduction of VL on Dried Blood Spots using venous blood
- Initially prepared by the laboratory
- Now being prepared by nurses at the clinic ; meaning patients don't have to attend twice
- Future possibilities to do finger prick



Overcoming the VL Access barriers
Step 2: Cost



Overcoming the VL Access barriers
Step 3: Developing a Clinical algorithm



Algorithm 14: Triggered viral load use and switch to second line

Clinical failure (after 12 months ART)
Any new Stage 2–4 condition

Immunological failure (after 12 months ART)
CD4 < 100
CD4 < baseline
CD4 drop > 30% from the peak CD4 result since on ART

Poor adherence suspected
Proven missed pills < 95% adherence
Proven defaulting
Suspected drug interactions

CD4 drop < 30%: No special intervention

Enhanced adherence according to patient needs

Ongoing poor adherence

Check Viral Load + adherence counselling
Check CD4 if last CD4 result > 3 months ago

If Viral Load >400 copies: 3 months enhanced adherence

If VL <400 copies: Continue 1st line ART and 6-monthly CD4

Repeat Viral Load

Viral Load <400: Do **not** switch. Continue routine monitoring with 6 monthly CD4

Viral Load 400 -5000: Do **not** switch, continue 1st line. Repeat Viral Load in 6 months. Enhanced adherence if needed

Viral Load >5000: **Switch** to 2nd line after team discussion. NB Consider Log drop. If 0.5 or greater consider continue 1st line and repeat VL 3 months

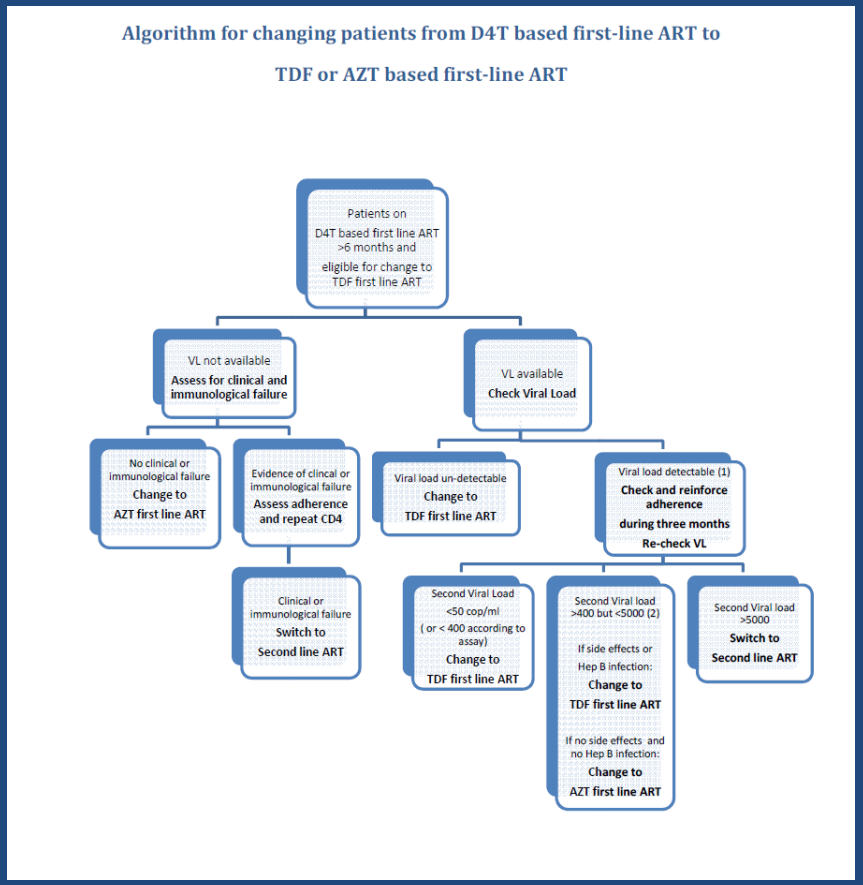
The definition of lower than detectable limits (LDL) can vary depending on the laboratory used. All switches to second line should be after a minimum of 12 months on ART.

If TDF is in the first line check Hep B status and consult doctor.

Notes: HBsAg should be checked before considering a discontinuation of TDF, since stopping TDF could cause a serious flare of hepatitis.

If routine viral load becomes available the same algorithm flow will be followed. I.e If VL is detectable 3 months of adherence support will be given and the VL repeated. If VL is > 5000 copies/ml then the patient will be switched to second line. N.B remember to consider the log drop.

Antiretrovirals (ARVs)



Algorithm for changing patients from D4T based first-line ART to TDF or AZT based first-line ART

Patients on D4T based first line ART >6 months and eligible for change to TDF first line ART

VL not available
Assess for clinical and immunological failure

VL available
Check Viral Load

No clinical or immunological failure
Change to
AZT first line ART

Evidence of clinical or immunological failure
Assess adherence and repeat CD4

Viral load un-detectable
Change to
TDF first line ART

Viral load detectable (1)
Check and reinforce adherence during three months
Re-check VL

Clinical or immunological failure
Switch to Second line ART

Second Viral Load <50 cop/ml (or < 400 according to assay)
Change to
TDF first line ART

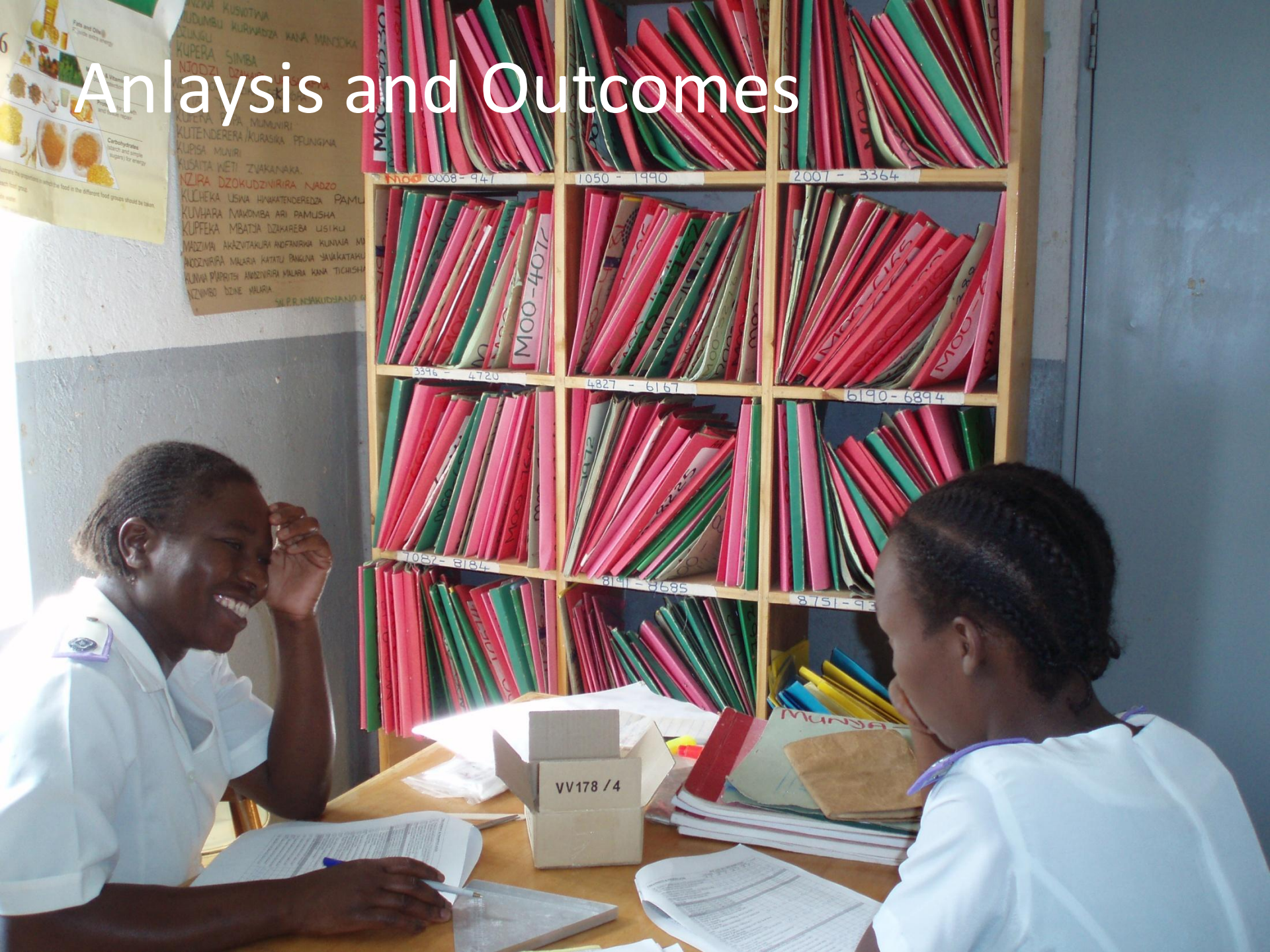
Second Viral load >400 but <5000 (2)

If side effects or Hep B infection:
Change to TDF first line ART

If no side effects and no Hep B infection:
Change to AZT first line ART

Second Viral load >5000
Switch to Second line ART

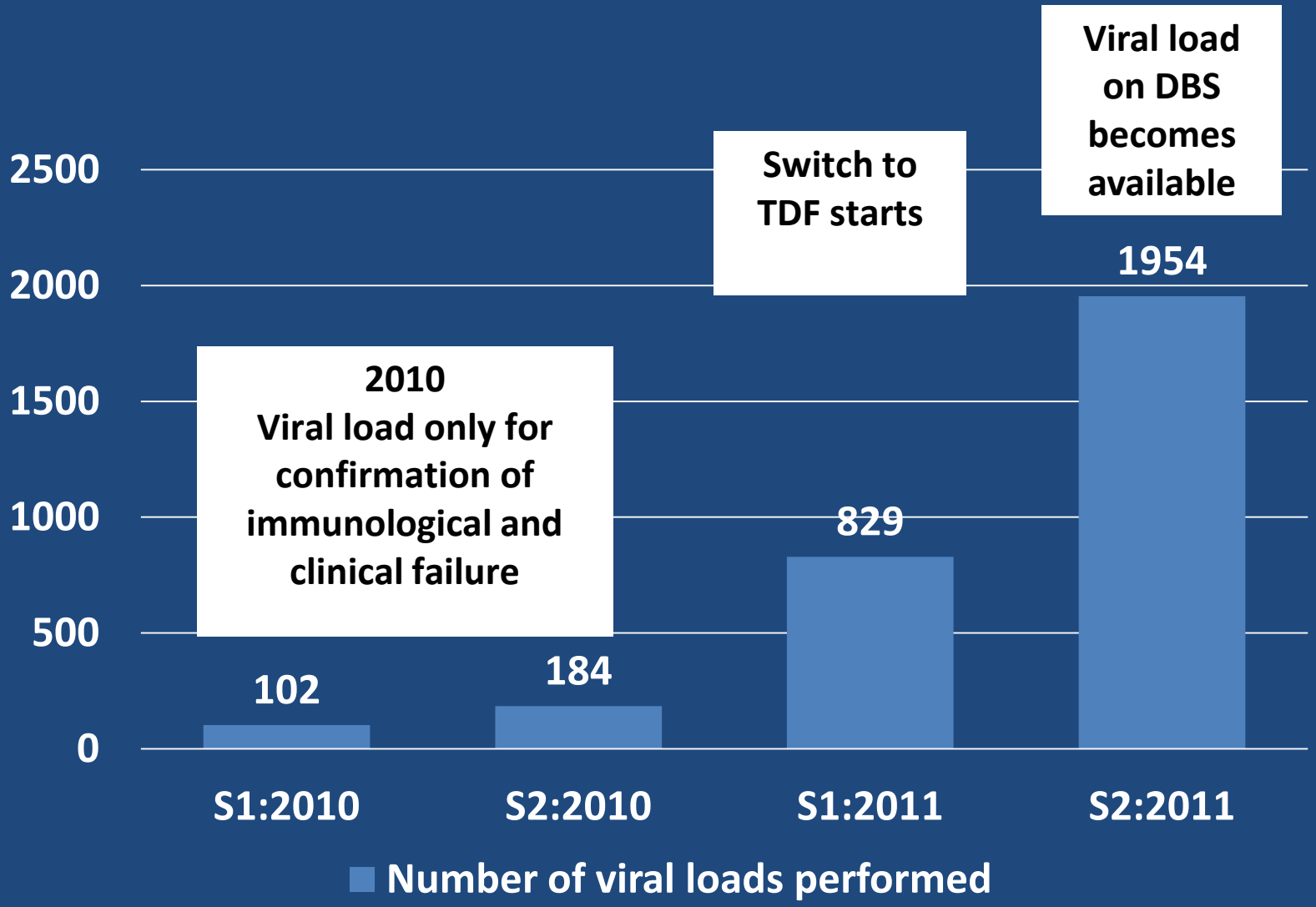
Anlaysis and Outcomes



Methods

- Data were entered prospectively into an electronic patient register
- Generalised linear models were used to estimate risk ratios to identify factors associated with viraemia among ART patients having viral load testing.

Increase in viral load tests During the phased implementation of TDF



Baseline Characteristics of cohort

Baseline Variables	N = 655 (%) Median (IQR)
Age	→ 44 (36-52)
Women	→ 412 (63%)
Median duration on ART	→ 3.2 years (1.9- 4.3)

Baseline Characteristics of cohort

Baseline Variables	N = 1459 (%) Median (IQR)
Age	→ 39 (36-50)
Women	→ 963 (66%)
Median duration on ART	→ To do

What proportion were detectable?

	(N= 655)	Detectable (N)	% (95% CI)
Clinical failure	24	8	33 (13-53)
Immunological failure	262	110	42 (36-48)
Side effects	369	111	30 (24-34)

What proportion were detectable?

	(N= 1459)	Detectable (N)	% (95% CI)
Suspect failure	544	169	31.1 (36.3 – 46.0)
Side effects	504	129	25.6 (21.8 – 29.6)
Routine switch	691	148	21.4 (23.5 – 31.2)
Total	1459	446	30.6 (28.2- 32.9)

Risk factors for failure

Risk of Having a detectable viral load	Risk Ratio (95%CI)	P value
Immunological Failure	1.28 (0.81-2.06)	0.29
Side Effects	1.06 (0.66-1.68)	0.81
On ART > 4 years	1.36 (1.03- 1.81)	0.03

Discussion

- **In cohorts who have not had access to routine viral load up to 30% may be detectable when viral load is introduced**
- **How many could return to undectable after an adherence intervention ? (39-50%)**
- **Counselling resources and access to second line drugs need to be prepared before scale up of viral load**

Discussion

- **Clinical and immunological definitions of treatment failure misclassified many patients as seen in a number of other studies (*Mee et al, Moore et al, Chaiwarith et al*)**
- **Effects on resistance if switching from stavudine to tenofovir on a failing regimen are not clear**
- **If Viral load is not available for all one strategy could be to prioritise those on ART > 4 years**
- **Most difficult/relevant (?) question: what is impact of this on morbidity and mortality??**

Take Home Message

Scaling up viral load in resource poor settings is possible now.....

Acknowledgements