Approach to pharmacovigilence, Western Cape Province, South Africa

Provincial Government of the Western Cape

Departments of Public Health and Pharmacology, University of Cape Town

Médecins Sans Frontières

Background

- Pilot ART programmes started in 2001, expansion to 43 sites since mid-2004
- 15,000 patients on ART at present
- 50,000 anticipated to be on ART in 2010
- All funding directed through government, including GFATM

Routine monitoring

1) Output reporting – monthly aggregates of total and new patients to inform resource planning

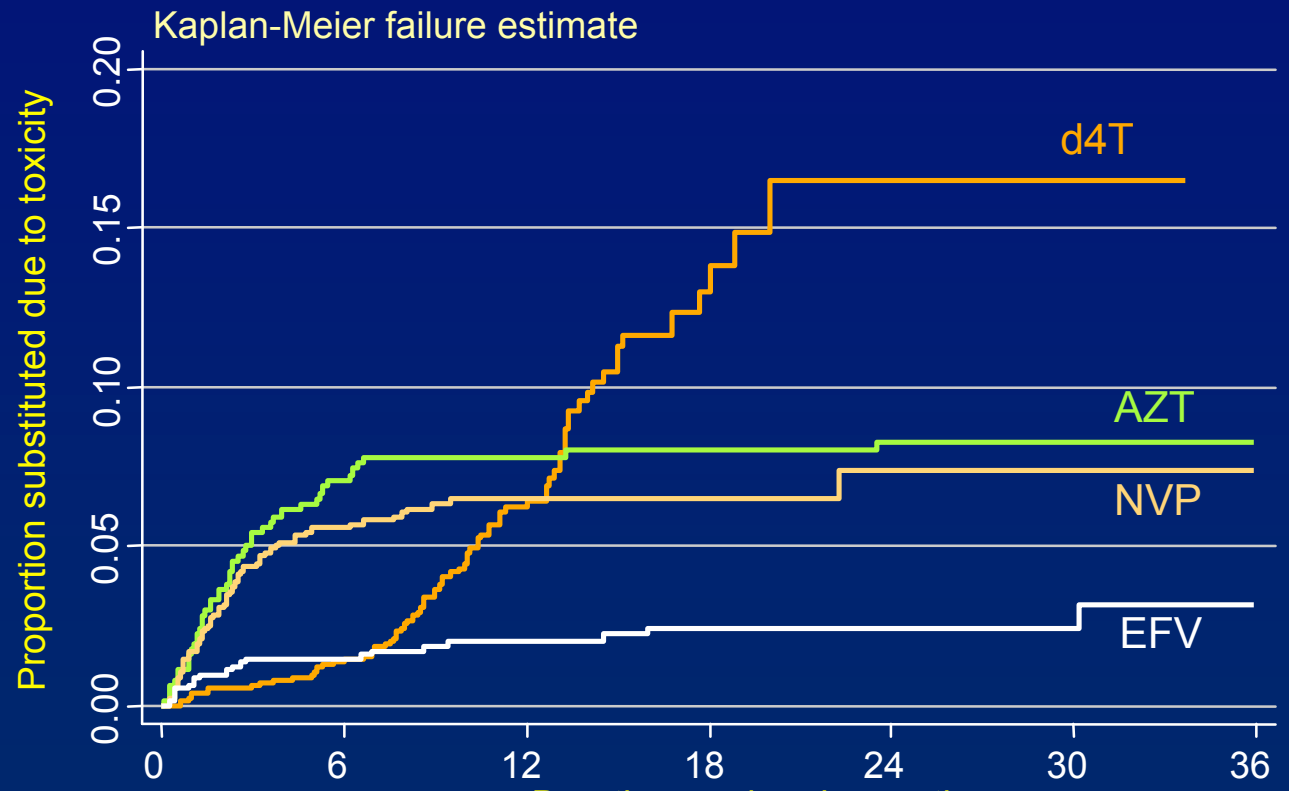
2) Outcome reporting – quarterly cohort reporting based on registers along the lines of WHO guidelines. Some of the bigger sites have patient information systems from which the reports are drawn *Mortality, LTF, Second-line, Laboratory outcomes*

3) Sentinel sites for detailed data to inform long-term programme planning = cohort studies – eg. Khayelitsha, Gugulethu

4) Special studies - eg. Case-control studies on virological failure and lactic acidosis

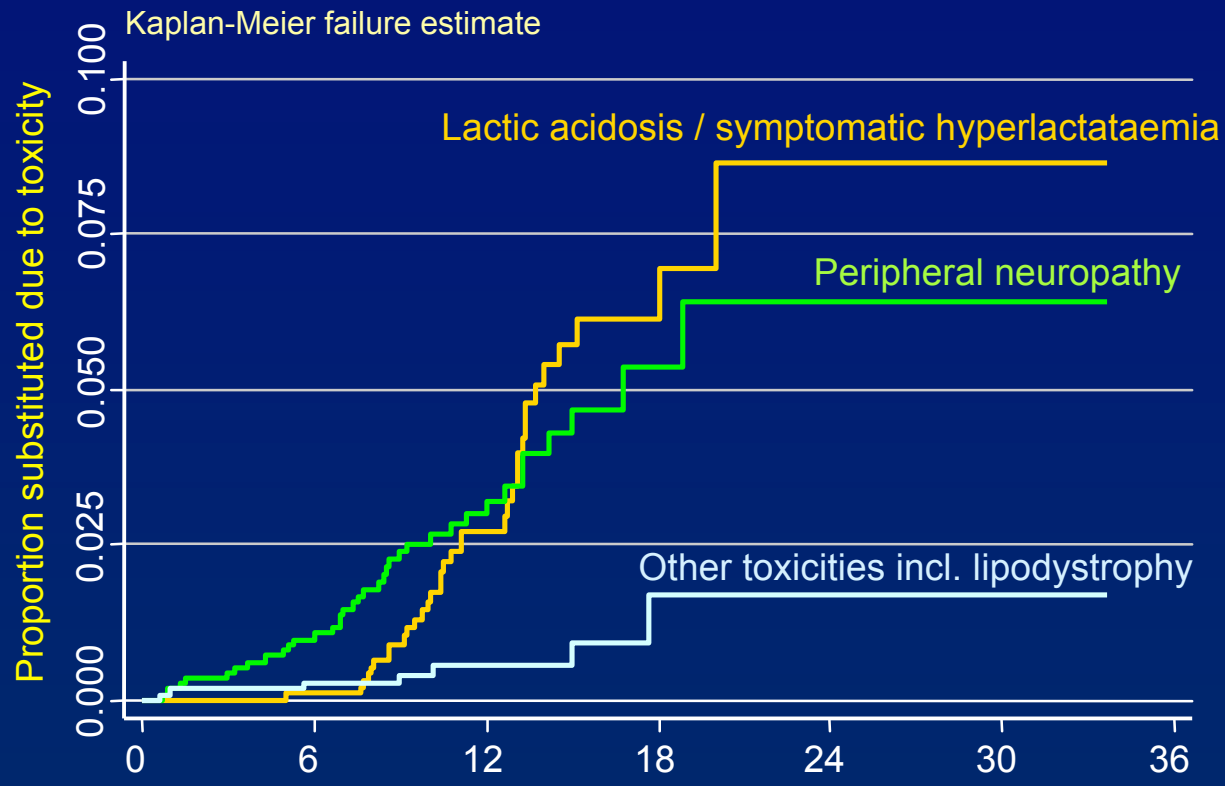
5) Enhance passive reporting of adverse events

Cohort example - Substitutions due to toxicity by drug



	n							Changed by 36 months (%, 95% CI)
d4T	1228	1065	471	113	18	9	5	16.5 (12.0-22.6)
AZT	639	497	442	417	306	205	132	8.3 (6.3-10.9)
NVP	977	828	385	129	104	89	63	7.4 (5.4-10.1)
EFV	967	790	558	423	245	139	81	3.1 (1.8-5.5)

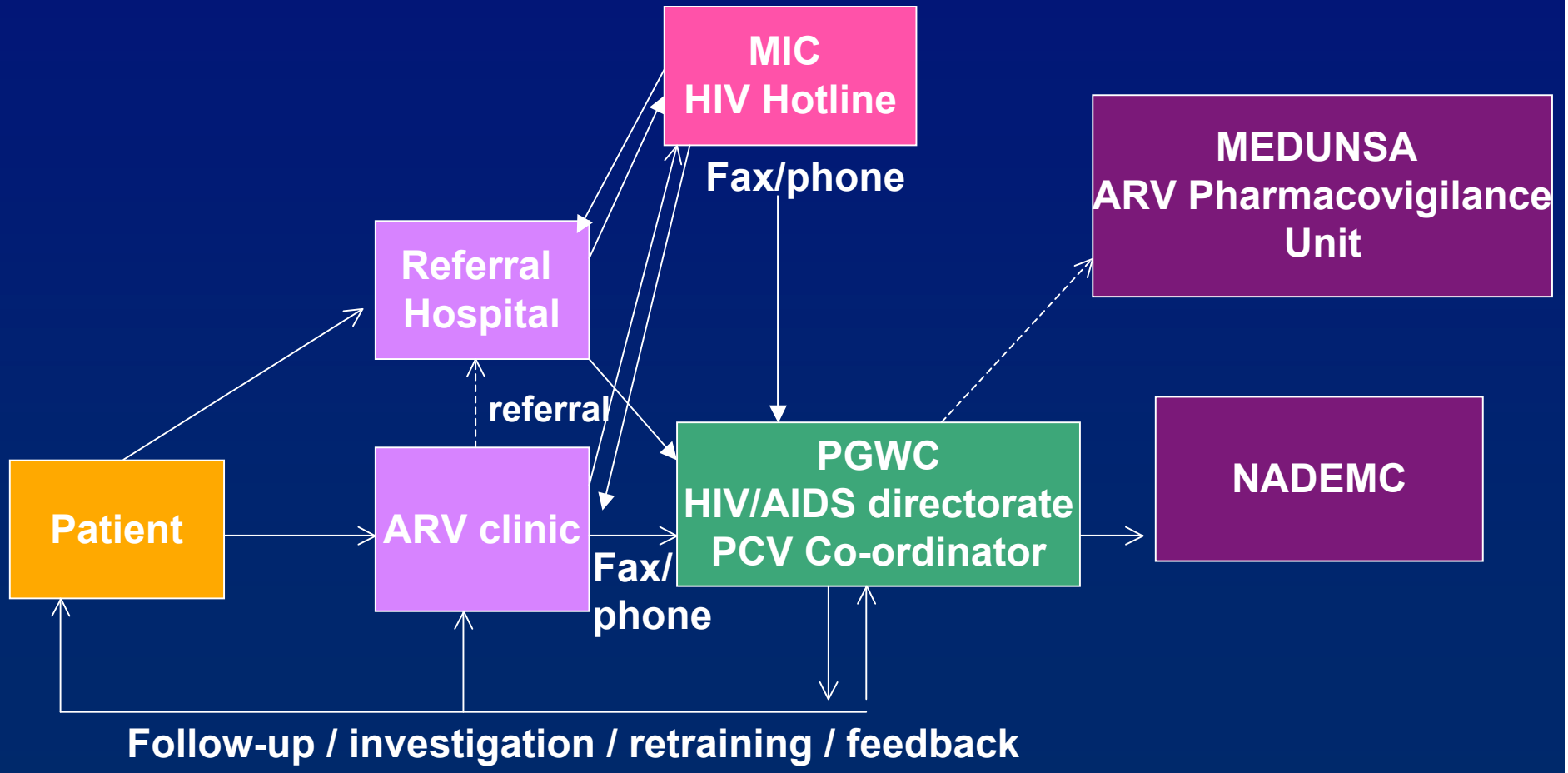
Cohort example - Causes of toxicity-driven substitutions in patients on stavudine



Reason for subst.	n							Changed by 36mo (%, 95% CI)
Hyperlactataemia/LA	1228	1074	484	118	20	11	6	8.7 (5.3-14.0)
Peripheral Neuropathy	1228	1068	486	120	19	9	5	6.4 (4.0-10.2)
Other	1228	1073	495	123	21	11	6	1.7 (0.6-4.6)
Combined	1228	1065	471	113	18	9	5	16.5 (12.0-22.6)

13th Conference on Retroviruses and Opportunistic Infections, Denver 2006

Enhanced passive surveillance



Slide provided by Ushma Mehta

Adverse event reporting form

Western Cape ARV Clinic Serious Adverse Event Reporting Form

Patient Initials _____ DOB _____ Gender ☐ Male

Weight _____ kg Height _____ cm ☐ Female

Treatment facility _____ Folder No. _____

Referral Hospital _____ Folder No. _____

Female patients only: Pregnant? ☐ Yes ☐ No ☐ Unknown

Medication history (circle suspected medicines and provide brand names where available)

Antiretroviral Medicines				Other Medication (including TB medication, herbal and traditional and over-the-counter medication)			
ARV	Dose	Date started	stopped	Medicine	Dose	Date started	stopped
Date ART was first commenced in this patient _____							

Adverse Event Details (Indicate with an "X" all that apply) (see back for case definitions of adverse events)

☐ Death *Suspected Cause of Death* _____

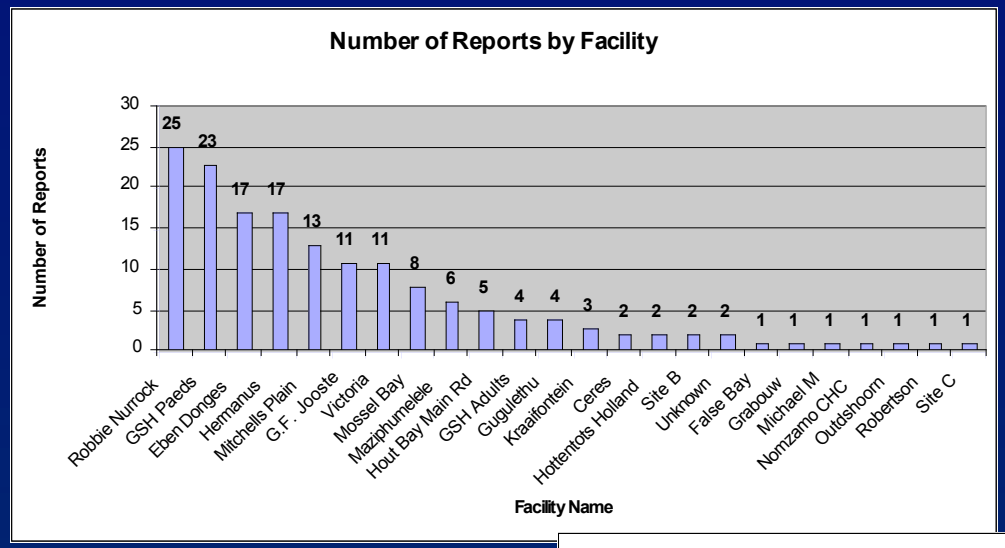
☐ Symptomatic hyperlactataemia

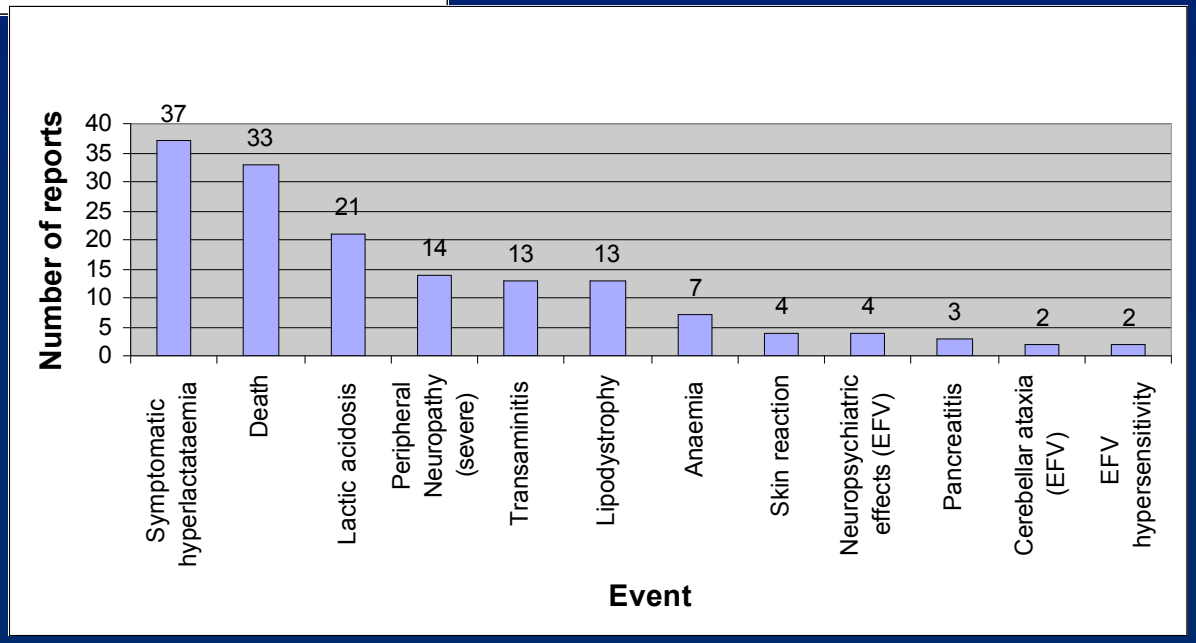
☐ Lactic acidosis

☐ Grade 3 or 4 transaminitis/ Symptomatic hepatitis

Lactate level	*Blood Gas results*

Performance of system to date





Courtesy of Ushma Mehta

Summary

- Stratified approach to routine monitoring, avoiding trying to do everything everywhere
- Cohort studies an important component but require additional resources
- Adverse event reporting achieves different objectives; is quicker, reflects clinical management and problems, and can identify new phenomena. Not intended to develop event incidence estimates
- Special studies a useful adjunct

Special studies

- 2 case control studies underway, one to look at risk factors for virological failure, one to look at risk factors for lactic acidosis
- Utilise the clinic registers as sampling frame
- Ability to aggregate more cases than the cohort studies alone, especially if draining via a referral hospital