

Transmission of XDR TB

Neel Gandhi, MD

Tugela Ferry Care & Research Collaboration (TF CARES)

Albert Einstein College of Medicine

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UNIVERSITY OF
KWAZULU-NATAL

Background



2006: 53 XDR TB cases in South Africa

- 52 of 53 (98%) died
 - median survival 16 days
- All HIV-infected, if status known
- Transmission of XDR TB likely
 - 51% never previously received TB treatment
 - 85% with genetically similar TB strains

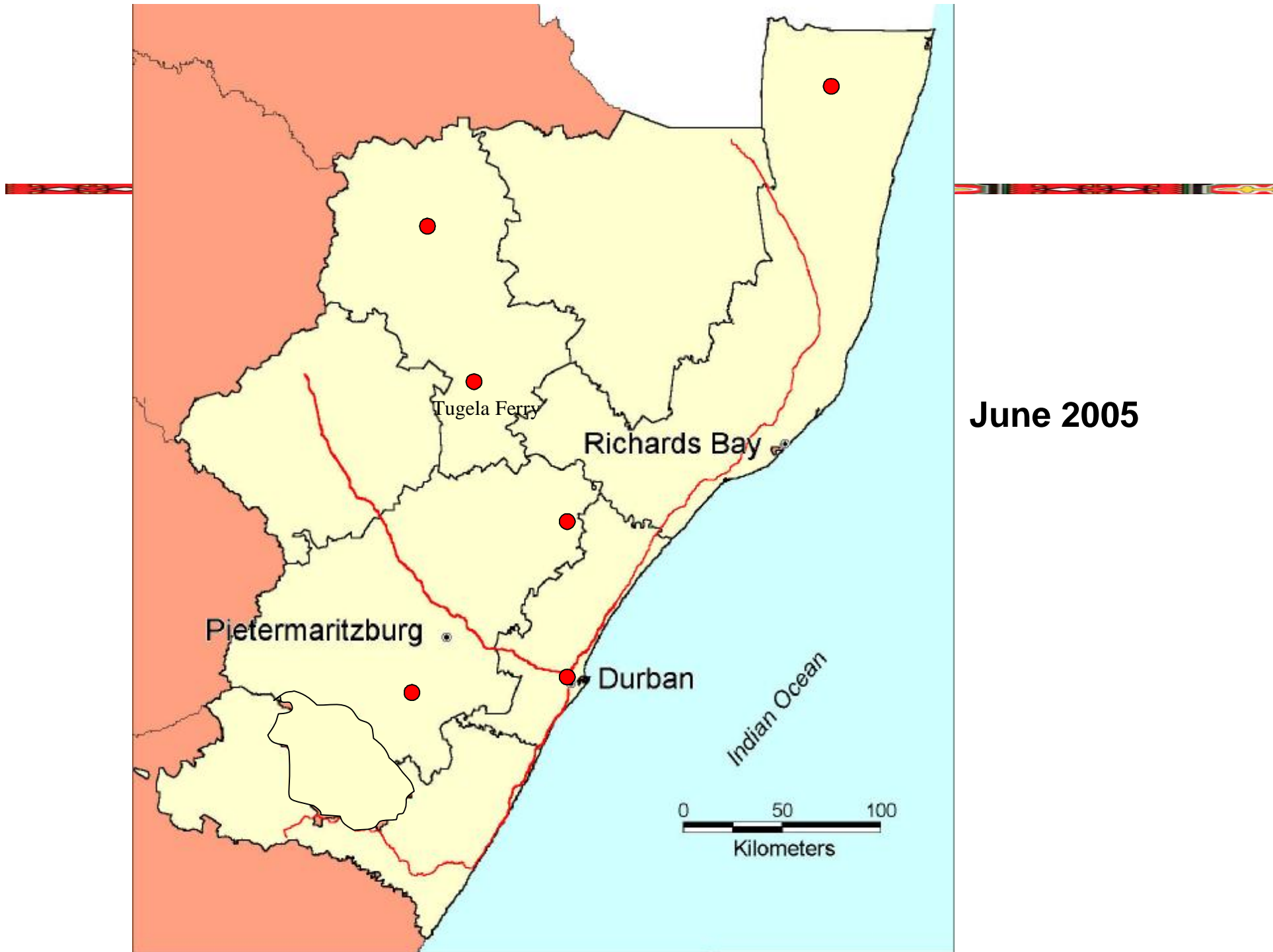
Local Outbreak vs Epidemic



- 2001-2002: MDR TB prevalence low: 2-4%
- 2006: KwaZulu-Natal: 2654 MDR TB cases
 - MDR TB Prevalence: 26 cases per 100,000
 - US 2005: 124 MDR TB cases total
Prevalence of any TB: <5 per 100,000

Rapid Emergence of MDR & XDR TB

- What can explain rapid rise in MDR TB cases?
- Emergence of XDR TB provides insights into rise of both MDR and XDR TB



June 2005

Pietermaritzburg

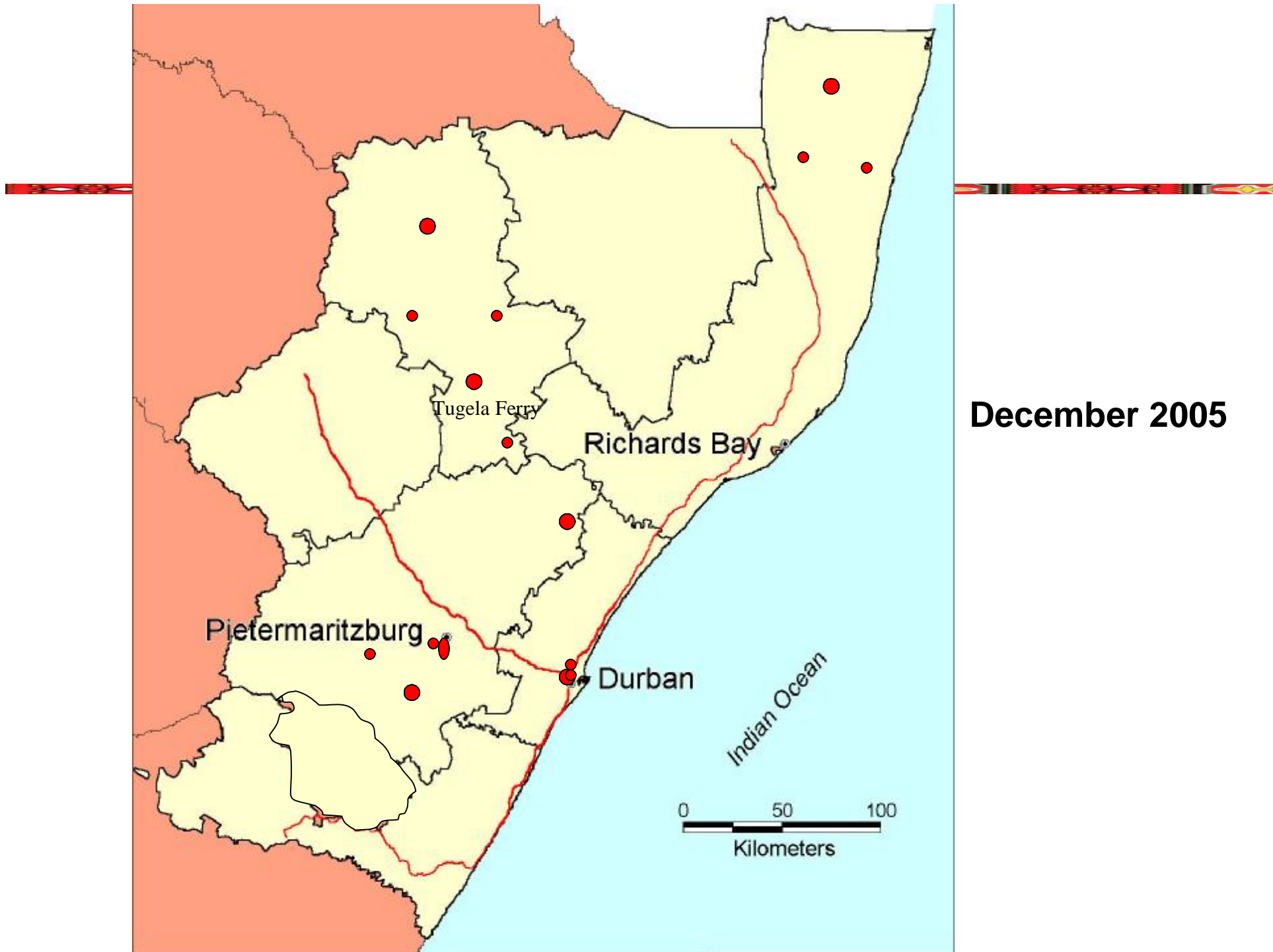
Richards Bay

Tugela Ferry

Durban

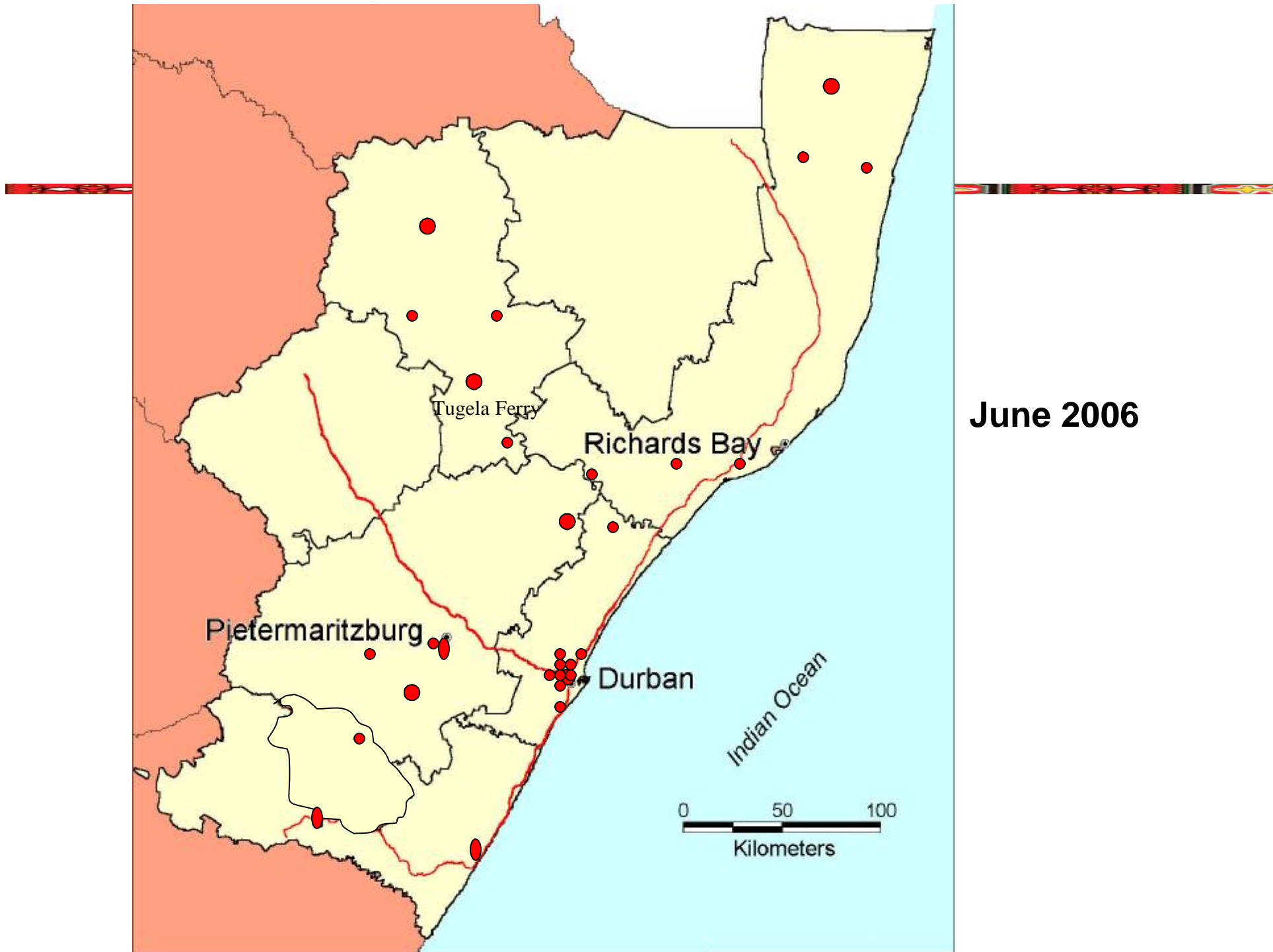
Indian Ocean

0 50 100
Kilometers



December 2005

0 50 100
Kilometers



June 2006

Pietermaritzburg

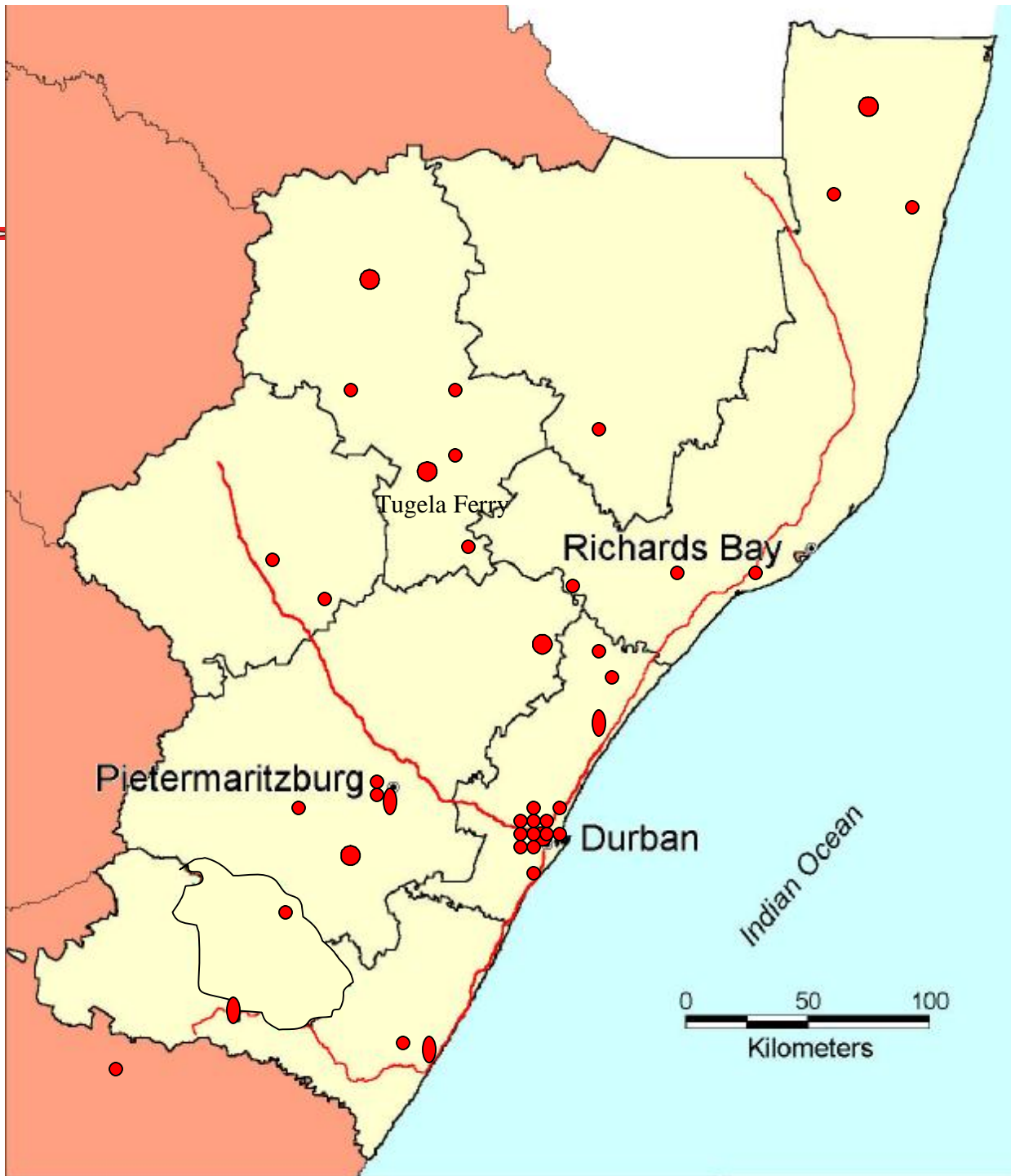
Tugela Ferry

Richards Bay

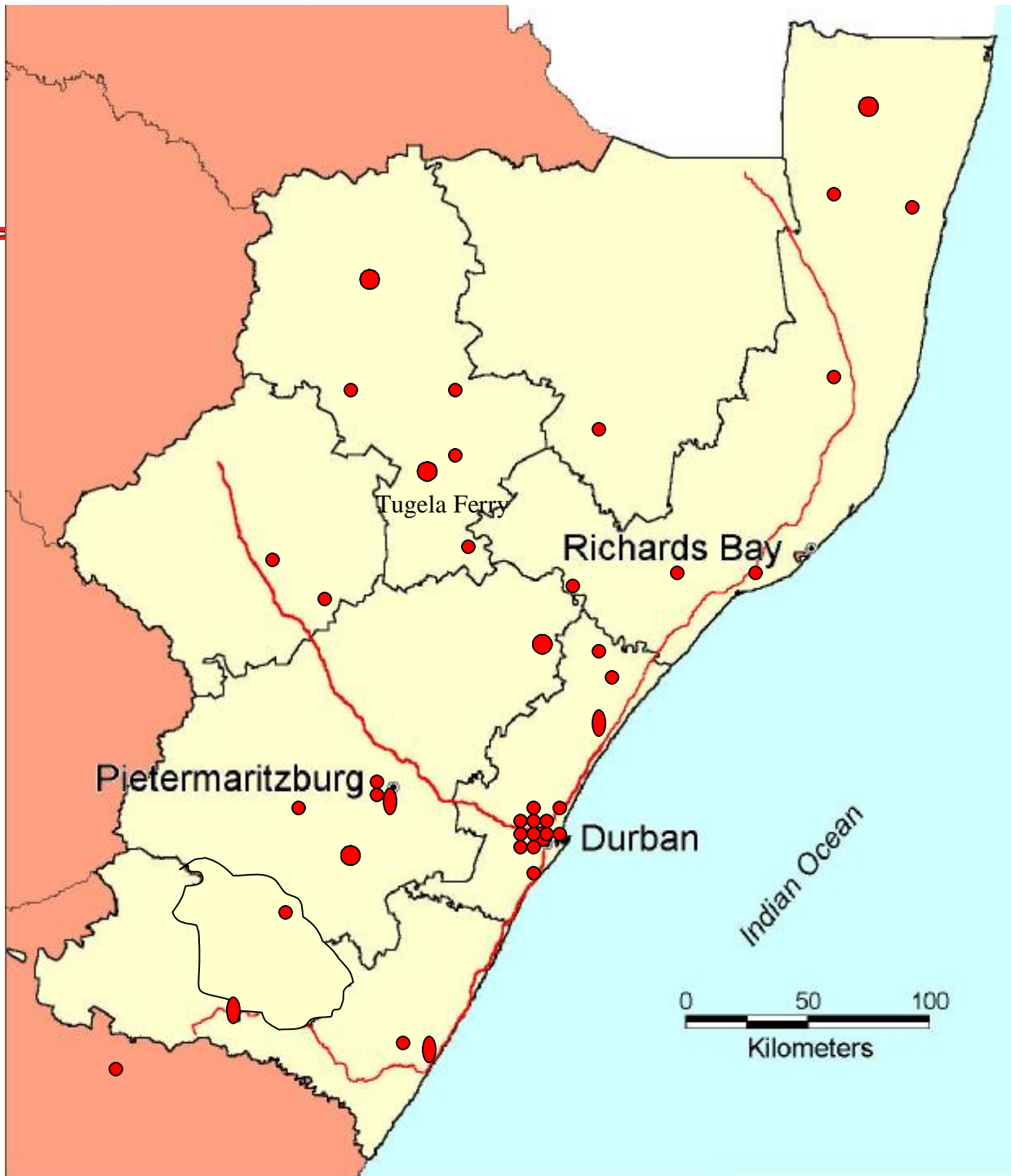
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Indian Ocean

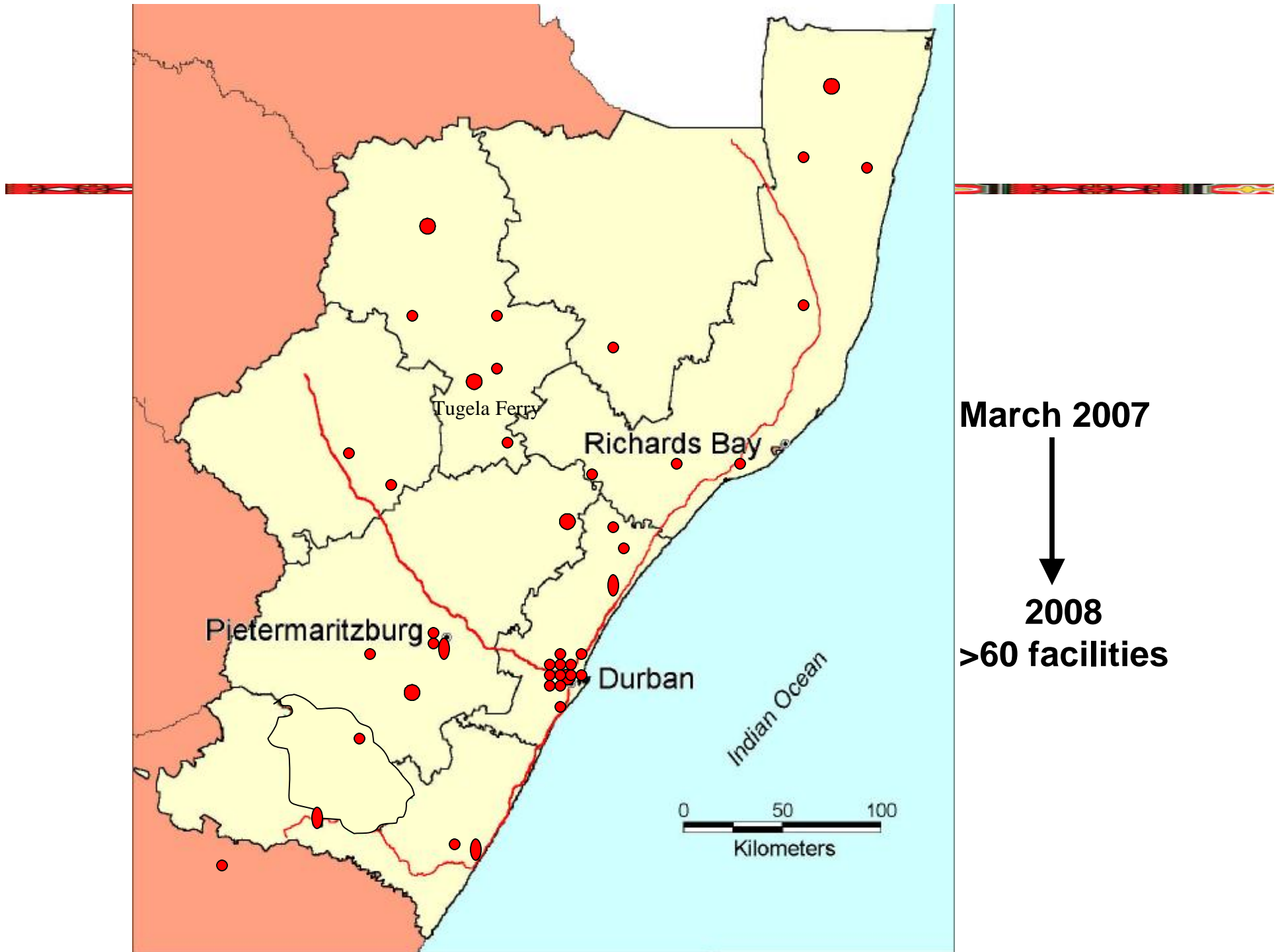
0 50 100
Kilometers



December 2006



March 2007



March 2007



2008

>60 facilities

MDR & XDR TB Widespread in South Africa



- XDR TB cases in all 9 South African provinces
- MDR and XDR TB prevalence rates are similar among all provinces
- XDR TB cases reported from all of South Africa's neighbors
 - Namibia, Botswana, Lesotho, Swaziland, Mozambique

What's driving this epidemic?



- Traditional Dogma
 - Selection for drug-resistant TB strains in setting of poor adherence or incorrect treatment
“Acquired or Amplified Resistance”
- Neglected mechanism
 - Transmission of drug-resistant TB strains
“Primary or Transmitted Resistance”

Acquired vs. Transmitted Resistance



- Acquired or amplified resistance may explain original genesis of first XDR TB strains
- Current magnitude and spread of XDR TB difficult to explain by acquired resistance alone
 - Tugela Ferry alone 2005-2007: 382 XDR TB cases
- High likelihood of primary or transmitted resistance
 - 30% Never previously treated for TB
 - Prior Treatment Relapse: due to new infections
 - Majority were cured or completed treatment course
 - Molecular genotyping data

Transmission of MDR & XDR TB?



- Molecular fingerprinting to determine acquired vs primary resistance in relapses with MDR and XDR TB
- Compared genotypes between initial susceptible isolate and follow-up MDR or XDR TB isolate
 - If genotypes differ, resistance due to new infection
 - If genotypes same, resistance due to acquired resistance from ineffective treatment

Baseline Characteristics



17 patients: susceptible TB → MDR or XDR TB

- Baseline & follow-up isolates available for genotyping
- 15 of 17 tested for HIV: 100% HIV-infected
- Inpatients and outpatients enrolled
 - 17 (100%) hospitalized at time of susceptible TB or before relapse with MDR or XDR TB
 - Median 25.5 days in hospital

Genotyping Results



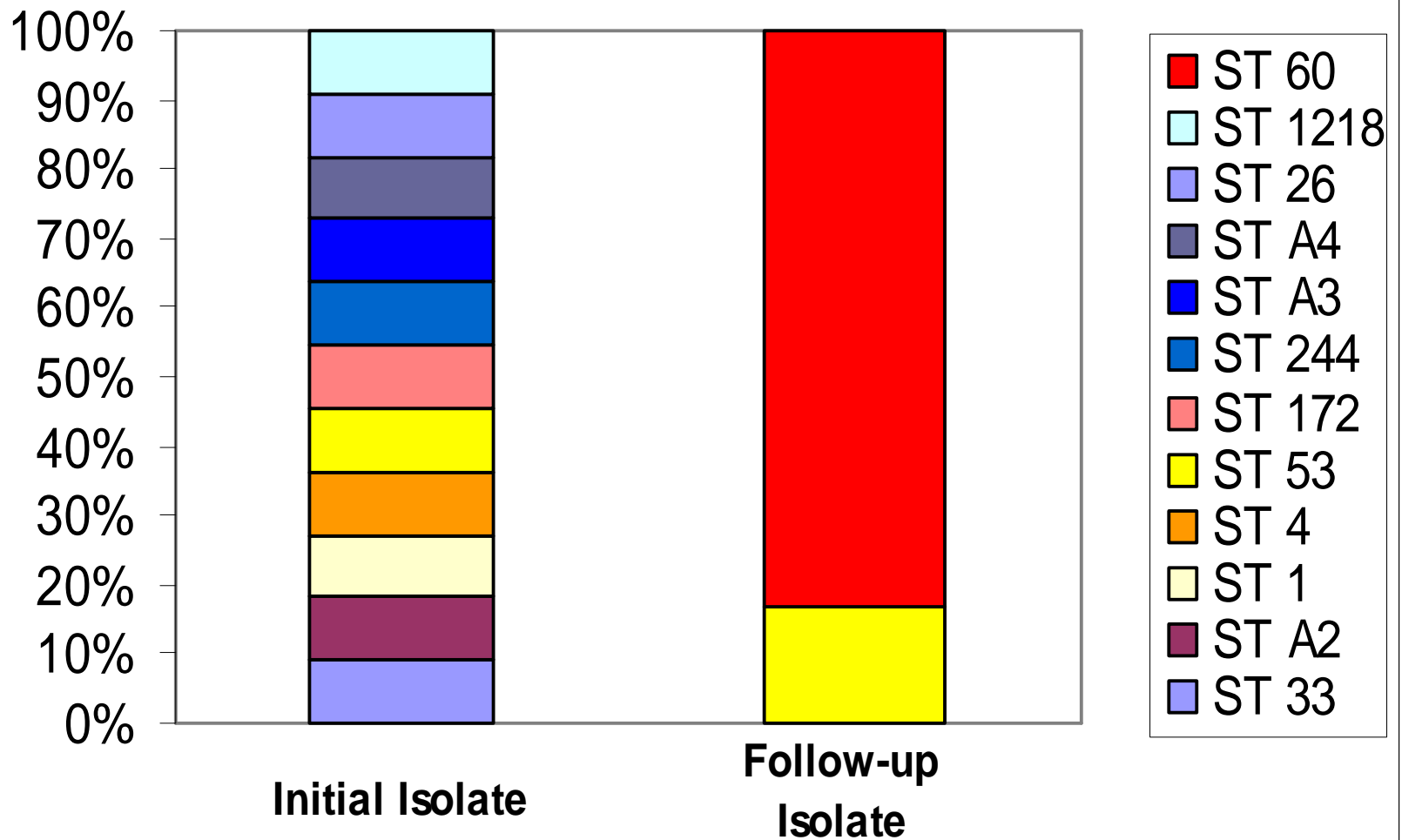
- All 17 (100%) follow-up MDR/XDR genotypes different from initial isolate
 - All cases re-infected with MDR or XDR strain
 - No cases of acquired resistance

Four TB Strains in Single Patient

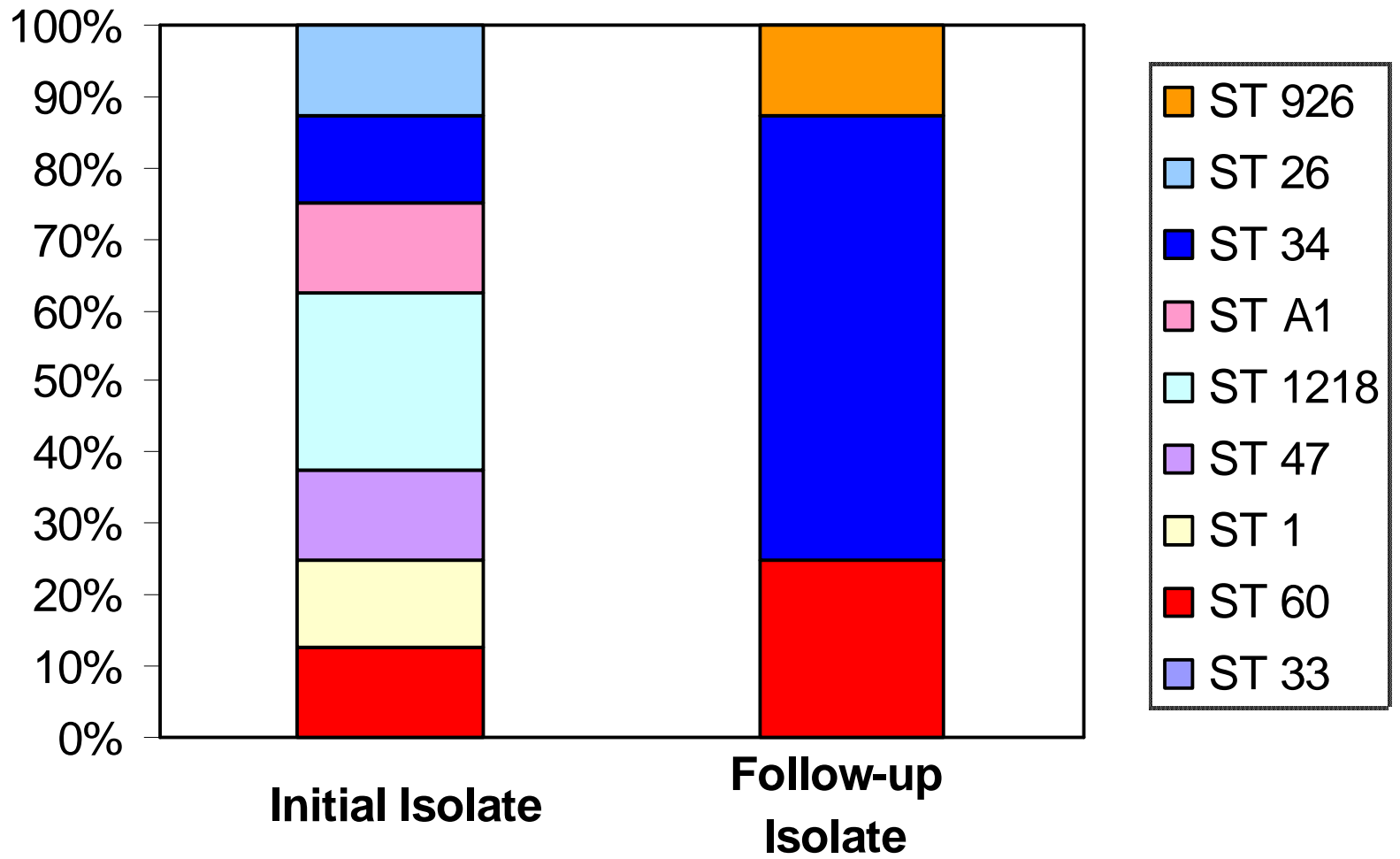
Susceptible TB à MDR TB à XDR TB



Genotypes of Patients with XDR TB Relapse



Genotypes of Patients with MDR TB Relapse



Conclusions



- Transmission of drug-resistant strains is the principal source of MDR & XDR TB in South Africa
- High rates of HIV co-infection and hospitalization may have contributed to risk
- Re-infection with MDR and XDR TB attributable to relatively few TB strains
 - Suggesting common sources of transmission

Implications



- Efforts must focus on creating infection control programs to prevent the transmission of drug-resistant TB strains
 - Most settings worldwide with no infection control
- Early diagnosis necessary to facilitate infection control
 - Hampered by lack of laboratory capacity and lack of simple, rapid diagnostic test
- Further studies to characterize transmission patterns needed

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