Article: *HIV Coinfection in Multidrug- and Extensively Drug-Resistant Tuberculosis Results in High Early Mortality*

1. **Overview**
   - Retrospective, observational research study
   - Commentary
   - Peer reviewed
   - Major findings: “Mortality from MDR and XDR TB in this high HIV prevalence region is extraordinarily high, particularly within the first 30 days”

2. **Introduction**
   - **Issues:**
     - Specify which drugs are most often prescribed for TB/if isoniazid and rifampin are a part of that list (“MDR TB—whish is TB that is resistant to at least isoniazid and rifampin”)
     - Specify areas of the world/countries that are most affected by XDR TB (article only addresses that it has been reported in 55 countries worldwide since it first emerged in 2005) & do these areas also have low/high HIV prevalence?
     - Provide further background knowledge of the causes of MDR TB or XDR TB
     - The introduction overall addresses the current literature and background of MDR/XDR TB well & properly sources the information
     - Research questions are clearly described and address gaps in scientific literature
       - What are the characteristics of “mortality among 654 cases of MDR and XDR TB diagnosed at our study site in Tugela Terry, South Africa, since 2005”?
       - What is the “relationship between mortality and the extent of drug resistance”?
       - What are the “temporal changes in mortality and drug resistance patterns”?

3. **Methods**
   - **Issues:**
     - Address why pyrazinamide is not included in the standard DST panel
     - Clarify that “standard definitions” of MDR or XDR TB are adopted from CDC
   - Sampling strategy: reasonable for retrospective observation study
Medical record review (TB register maintained by TB treatment program at Tugela Ferry, validated by KZN Department of Health, found to be highly complete)

- Sample sizes are adequate: MDR TB (n=123), XDR TB (n=139)
- Statistical analysis is appropriate for posed research questions:
  - Calculation of simple frequencies and proportions of patients in each drug-resistance category
  - Cochran-Armitage test for linear trend over calendar years for each category
  - Primary outcome—time to death from date of sputum collection
  - Estimated survival rates in each resistance group and displayed in Kaplan-Meier survival curves
  - Combined groups with small sample sizes to “other MDR TB groups”
  - Significance was declared at two-sided alpha level of 0.05 and statistical analyses were conducted using SAS version 9.1

4. Results

- Issues:
  - There were 272 MDR TB and 382 XDR TB diagnosed from January 2005 to December 2007, but only 123 MDR TB and 139 XDR TB were analyzed… Why was only a subset of medical records reviewed? This should be specified
    - Vital statistics were only available for 265/272 of MDR TB and for 374/382 XDR TB, but why were only 123 MDR TB and 139 XDR TB reviewed?
  - Decimal points of P-values differ throughout the article, this should be kept consistent
- Results are overall comprehensive and cohere to the research questions
- Tables and figures are clear and appropriate for data presentation/response to research questions

5. Discussion/Conclusion

- This article adds relevant information to existing literature
  - Is the largest cohort of XDR TB cases reported to date worldwide
  - Demonstrated that both XDR TB patients and MDR TB patients in high HIV-prevalent area do not survive long enough to receive drug-resistant TB diagnosis and to initiate treatment
    - Other studies have been from low HIV-prevalent areas where few TB drug resistant individuals are coinfected with HIV
  - Reinforces need for greater allocation of resources to TB treatment programs
- Discussion points accurately correlate to the data presented in results section
- Articles provides public health suggestions for addressing the epidemic including universal culture and DST for all TB suspects, starting second-line TB treatment earlier, and implementing prevention efforts for MDR TB and XDR TB, especially in high-prevalence HIV areas
- Overall impression: Provisional acceptance (some minor changes required)