Impact of patient non-compliance on tuberculosis treatment regimens

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**Introduction**

Tuberculosis is a leading cause of death in the world today and infects about one third of the world’s population. WHO currently recommends a standard treatment for TB consisting of multiple drugs. Alternative drug combinations are also being investigated as possible regimens. Although the current standard treatment is fairly effective, due to factors including the long treatment time of tuberculosis, many patients do not follow the entire treatment regimen. This non-compliance could lead to the relapse of the patient and the emergence of drug-resistant TB.

**Objective**

To use a mathematical model that simulates TB drug treatment and patient non-compliance to investigate the effect of patient compliance with the three TB treatment regimens a percentage of the time.

**Possible Treatment Regimens**

- Standard - 8 weeks of isoniazid, rifampin, pyrazinamide, and ethambutol and 18 weeks of isoniazid and rifampin daily
- Remox 1 - 8 weeks of moxifloxacin, isoniazid, rifampin, and pyrazinamide and 9 weeks of moxifloxacin, isoniazid, and rifampin daily
- Remox 2 - 8 weeks of ethambutol, moxifloxacin, rifampin, and pyrazinamide and 9 weeks of moxifloxacin and rifampin daily

**TB and drug dynamics model**

\[
\begin{align*}
B_e &= r_B e (1 - B_e - B_i - B_x) - \delta_B e - \mu_B e - \mu_B e - \gamma_B e - \Sigma_B e
\\
B_i &= r_B i (1 - B_e - B_i - B_x) - \delta_B i - \mu_B i - \mu_B i - \gamma_B i - \Sigma_B i
\\
C_r &= -d_C C_r
\\
C_f &= f_C C_r (1 + C_0)
\\
I_f &= \frac{k_C C_r}{C_r + C_0} - \mu_B i - \gamma_B i - \Sigma_B i
\\
I_0 &= \frac{B_t}{N}
\\
\mu_B &= \frac{B_t}{N}
\\
\delta_B &= \frac{B_t}{N}
\\
\Sigma_B &= \frac{B_t}{N}
\\
\end{align*}
\]

**Results I**

The following graphs show examples of the time series of the bacteria and the drug for the standard treatment regimen at perfect adherence and 50% adherence.

- **Concentration of bacteria for perfect adherence to standard treatment**
- **Concentration of drugs for perfect adherence to standard treatment**

**Results II**

The graphs below show comparisons of the number of successes (<1 bacteria), apparent failures (>1 <100 bacteria) and apparent failures (>100 bacteria) for each treatment regimen at different percentages (100% - 50%) of adherence.

**Conclusion**

As the compliance to each treatment regimen decreases, the number of treatment success of each regimen also decreases. Remox 1 demonstrated the most number of treatment failures, while Remox 2 showed the least number of failures. Also, the differences among the number of failures as compliance to Remox 2 decreased were not as great as the differences among the number of failures to the standard treatment and Remox 1. This suggests that Remox 2 might be more forgiving towards patient non-compliance than the other two regimens.

In the future, more possible treatment regimens should be added to the model as well as other possible sources of non-compliance such as increasing non-compliance as the number of bacteria decreases and TB symptoms disappear.