CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

Using Multiple First-Line Therapies Against Malaria

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RESOURCES FOR THE FUTURE

PEI PRINCETON ENVIRONMENTAL INSTITUTE

BILL & MELINDA GATES foundation

Antimalarial Treatment Strategies Conference
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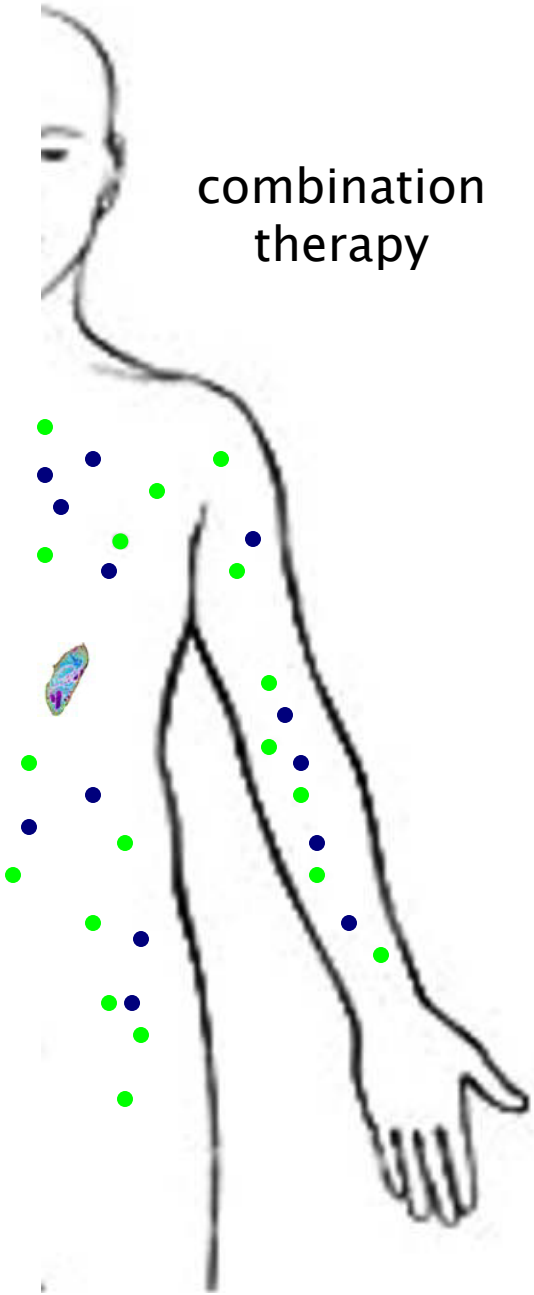
combination
therapy

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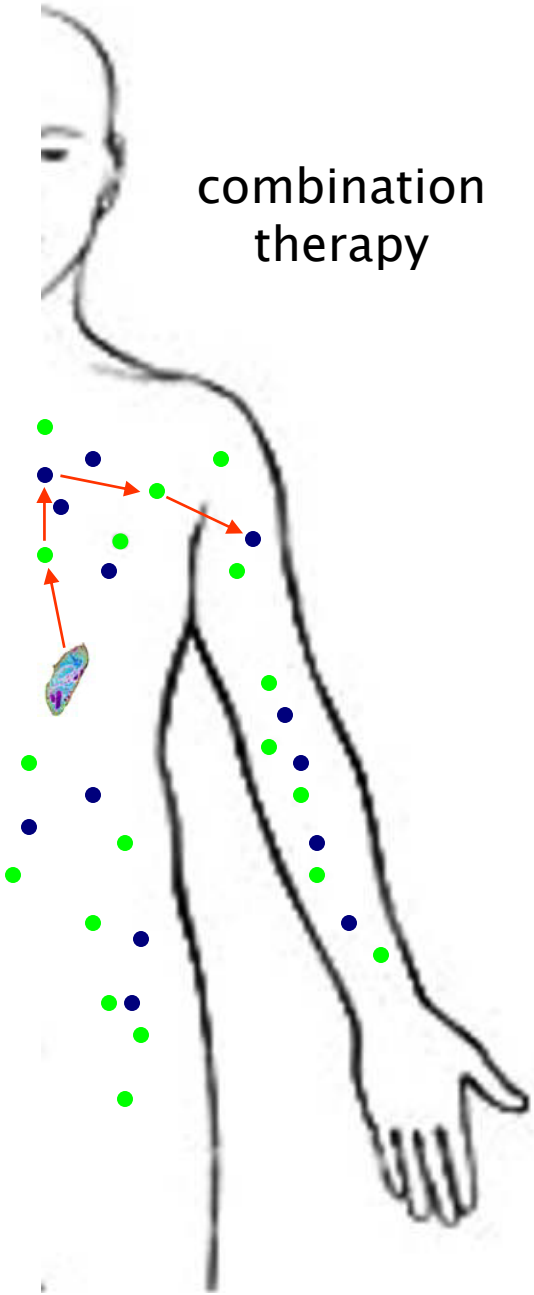
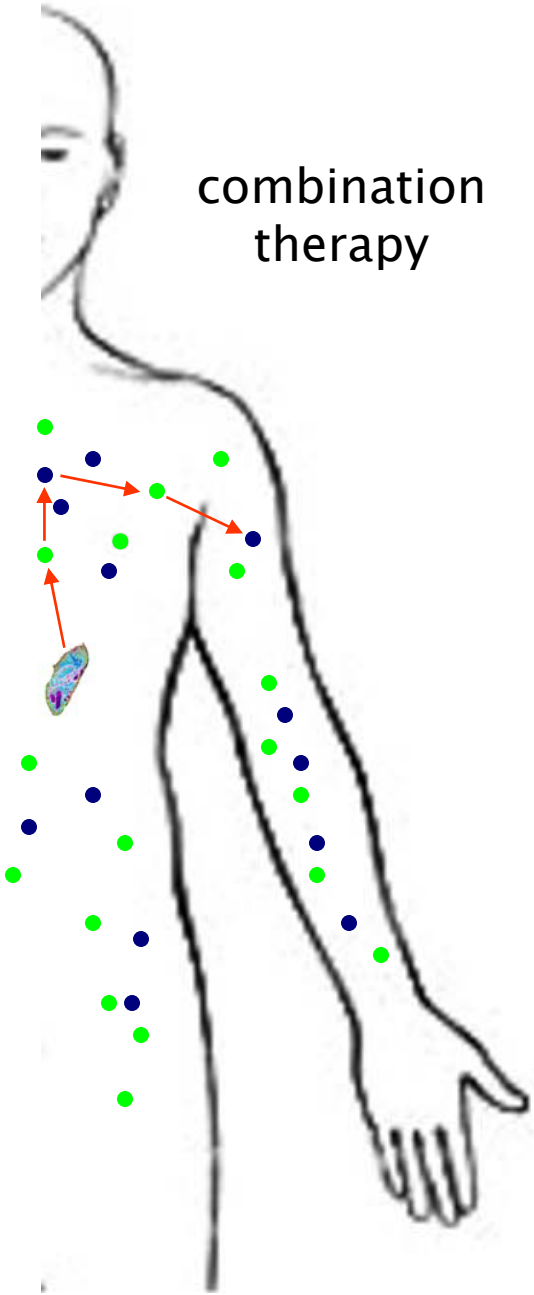
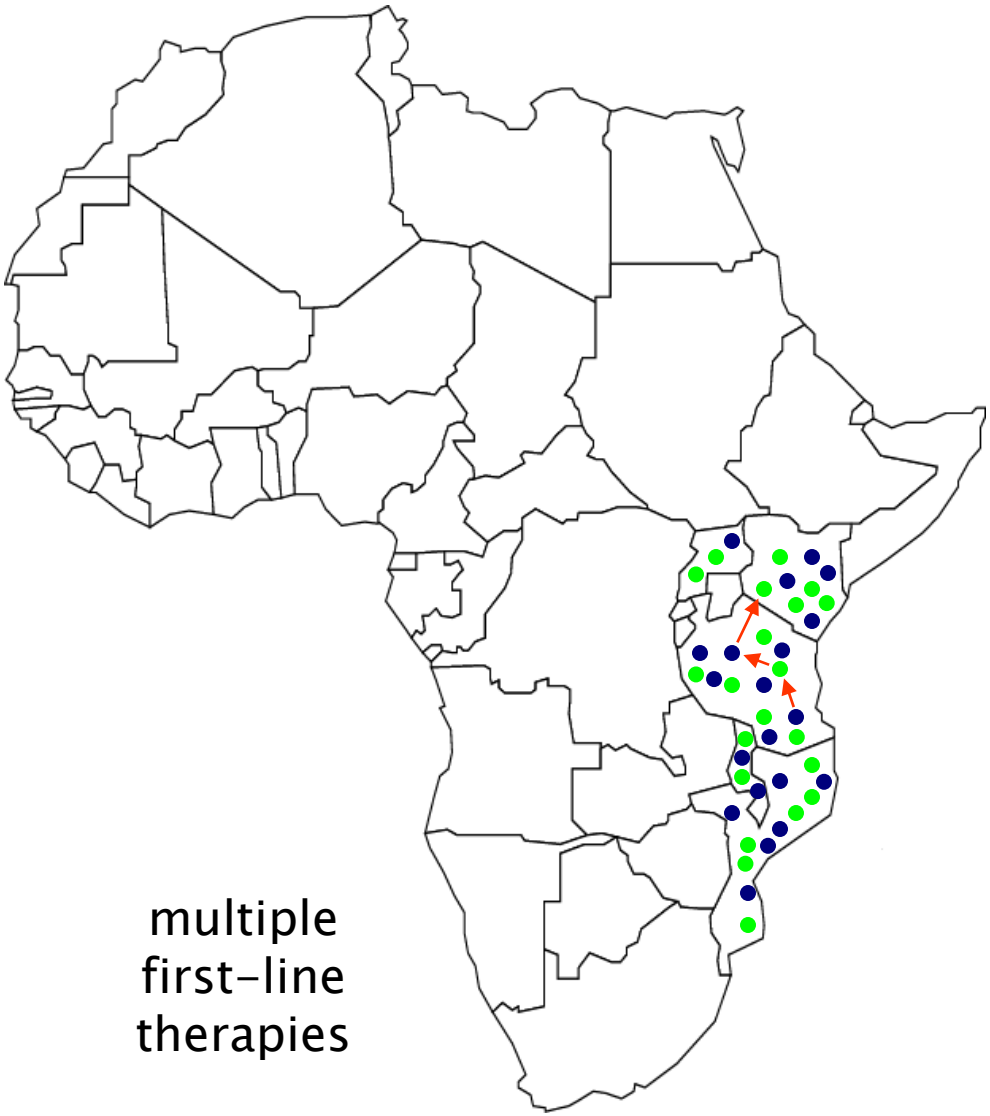
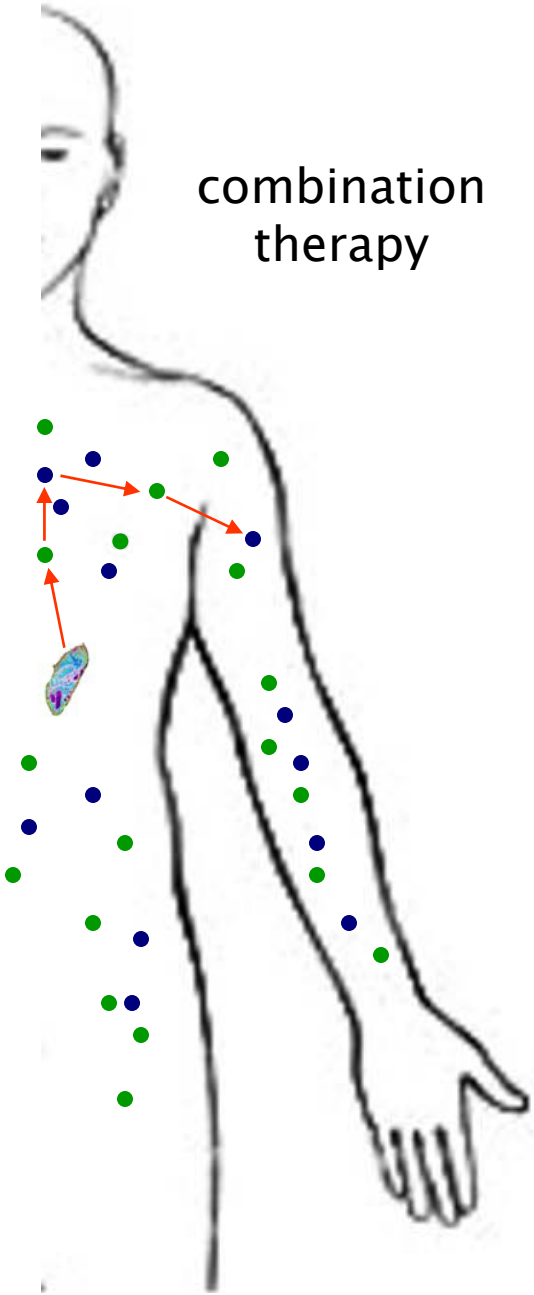
therapy

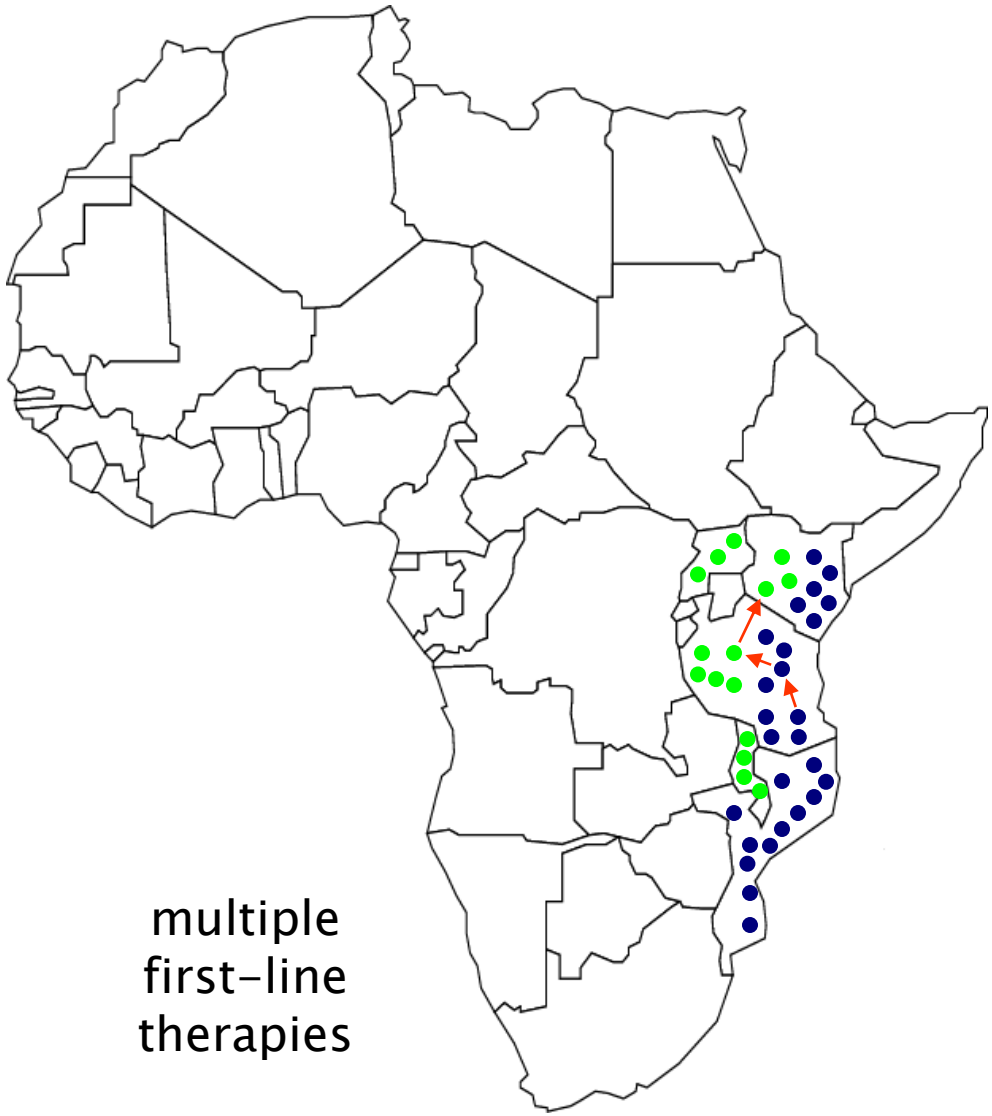



combination
therapy


multiple
first-line
therapies

combination therapy



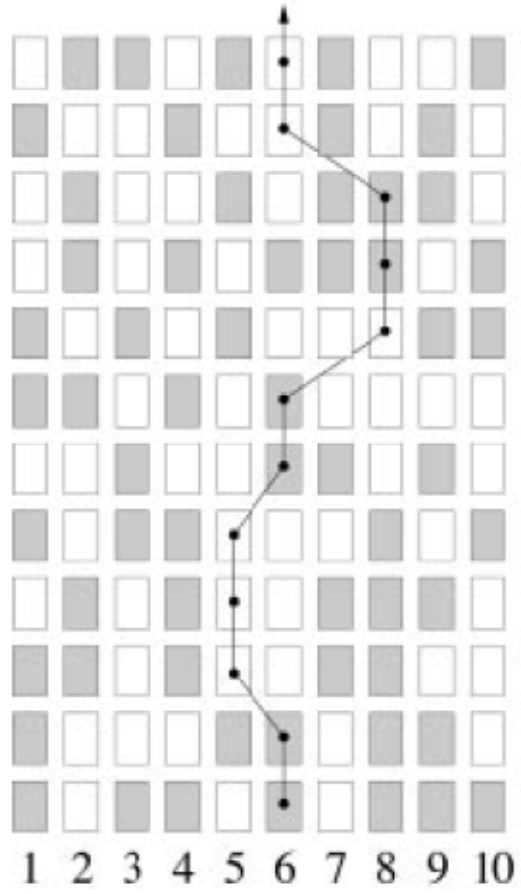


multiple first-line therapies

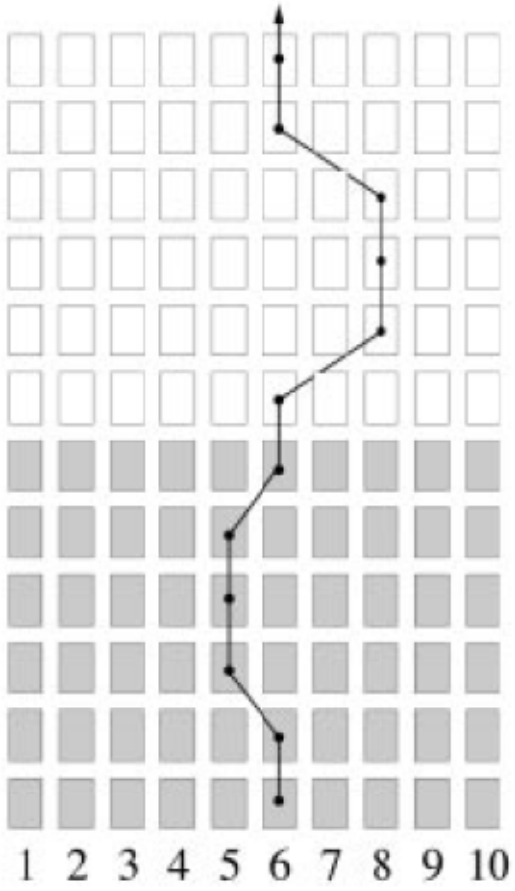
Using more drugs is advantageous.

Treatment Strategy Comparison

Effect #1



Multiple First-Line Therapies



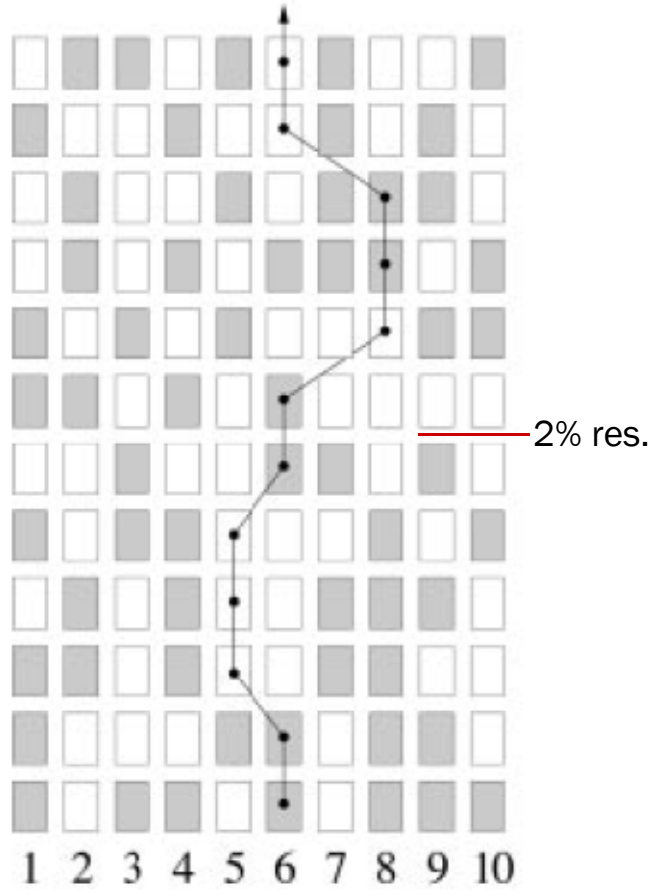
Cycling

pathogen experiences
less variable environment

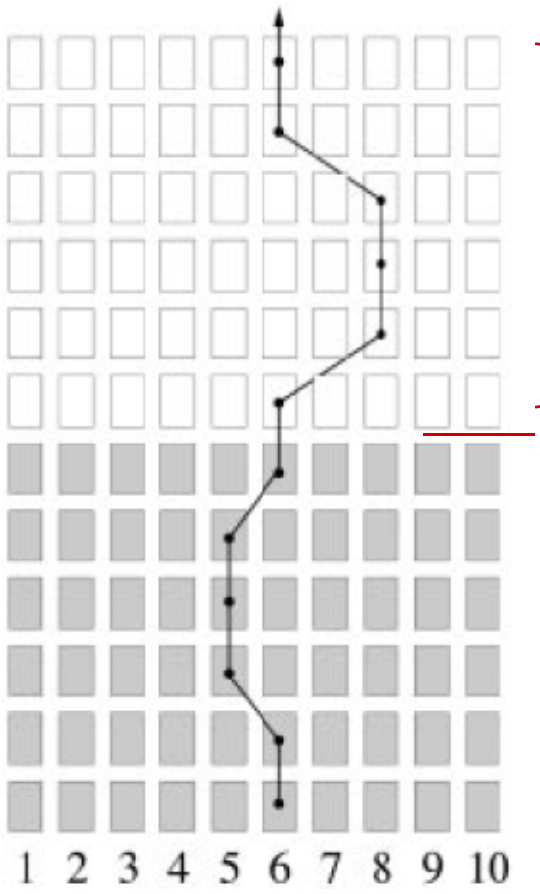
Bergstrom et al (2004)

Treatment Strategy Comparison

Effect #2



Multiple First-Line Therapies



Cycling

resistance evolution is much easier for the parasite

mean fitness of pathogen population is depressed

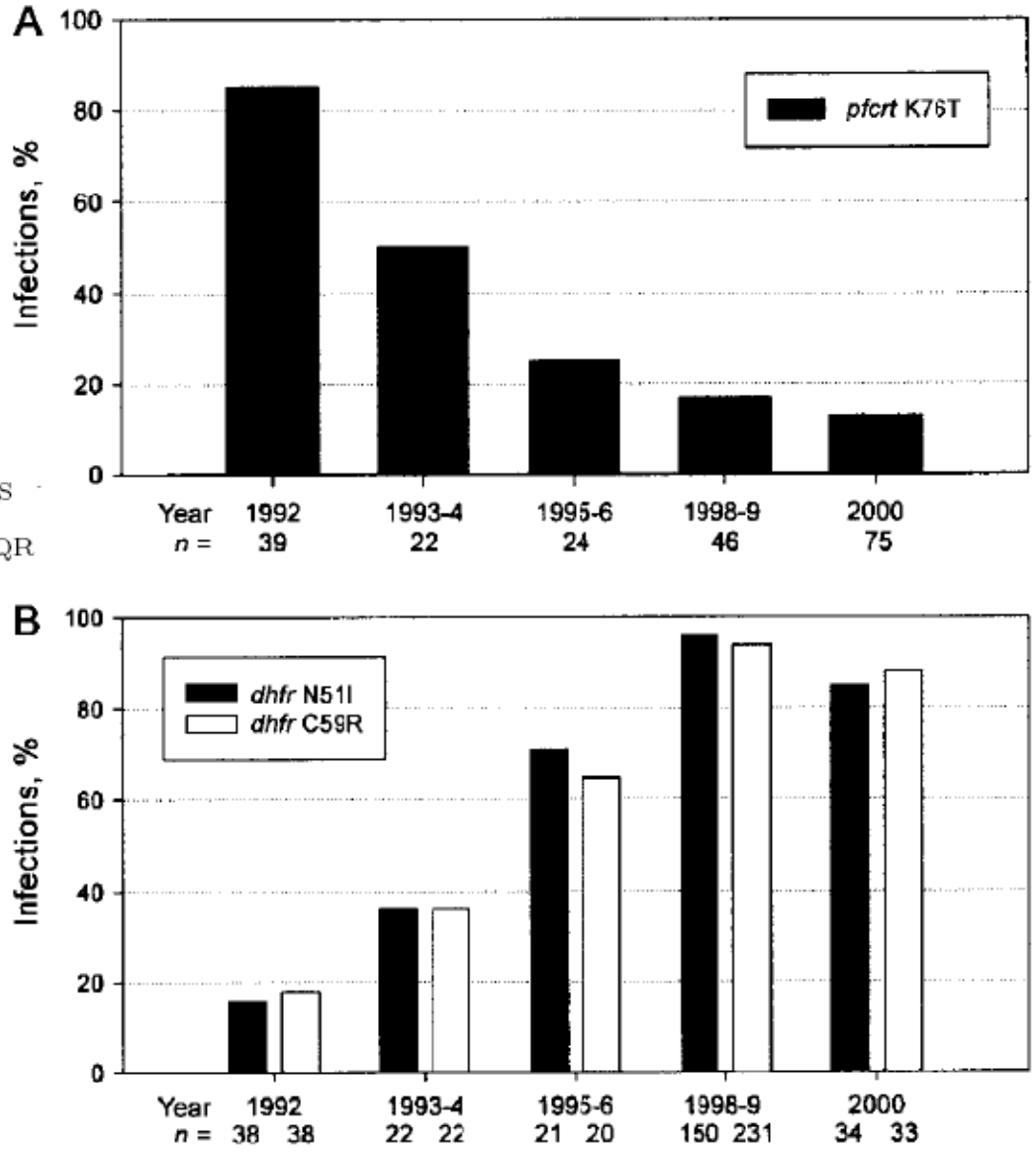
Bergstrom et al (2004)
Boni et al (2008)

Advantages of Deploying MFT

1. Delays emergence of resistant strains.
2. Slows down spread of resistance.
3. Reduces clinical burden and failed treatments.

Biological Cost of Resistance

$$\dot{A}_{\mathrm{SENS}} = \beta(1-\xi(f_{\mathrm{CQ}}+f_{\mathrm{SP}}))SA_{\mathrm{SENS}} - \nu A_{\mathrm{SENS}}$$
$$\dot{A}_{\mathrm{CQR}} = \beta(1-\xi f_{\mathrm{SP}})SA_{\mathrm{CQR}} - \nu(1+s_{\mathrm{CQR}})A_{\mathrm{CQR}}$$



Kublin et al (2003)

Biological Cost of Resistance

$$\dot{S}_0 = +g_0 S_1 - S_0 \sum_{\mathcal{Q}} h_{\mathcal{Q}} + \sum_{\mathcal{Q}} \nu_{|\mathcal{Q}} A_{\mathcal{Q},0}$$

$$+ \tau_F \sum_{\mathcal{U}} \sum_{\mathcal{Q}} \delta_{(\mathcal{U} \subsetneq \mathcal{Q})} \cdot (1 - \sigma_{|\mathcal{U} \setminus \mathcal{Q}|}) \cdot C_{\mathcal{U},\mathcal{Q},0}$$

$$\dot{S}_1 = -g_0 S_1 - S_1 \sum_{\mathcal{Q}} h_{\mathcal{Q}} + \sum_{\mathcal{Q}} \nu_{|\mathcal{Q}} A_{\mathcal{Q},1}$$

$$+ \tau_F \sum_{\mathcal{U}} \sum_{\mathcal{Q}} \delta_{(\mathcal{U} \subsetneq \mathcal{Q})} \cdot (1 - \sigma_{|\mathcal{U} \setminus \mathcal{Q}|}) \cdot C_{\mathcal{U},\mathcal{Q},1}$$

$$\dot{A}_{\mathcal{R},0} = (1 - \varepsilon_0)\, h_{\mathcal{R}}\, S_0 - (\gamma_0 + \nu_{|\mathcal{R}|} + g_1) A_{\mathcal{R},0}$$

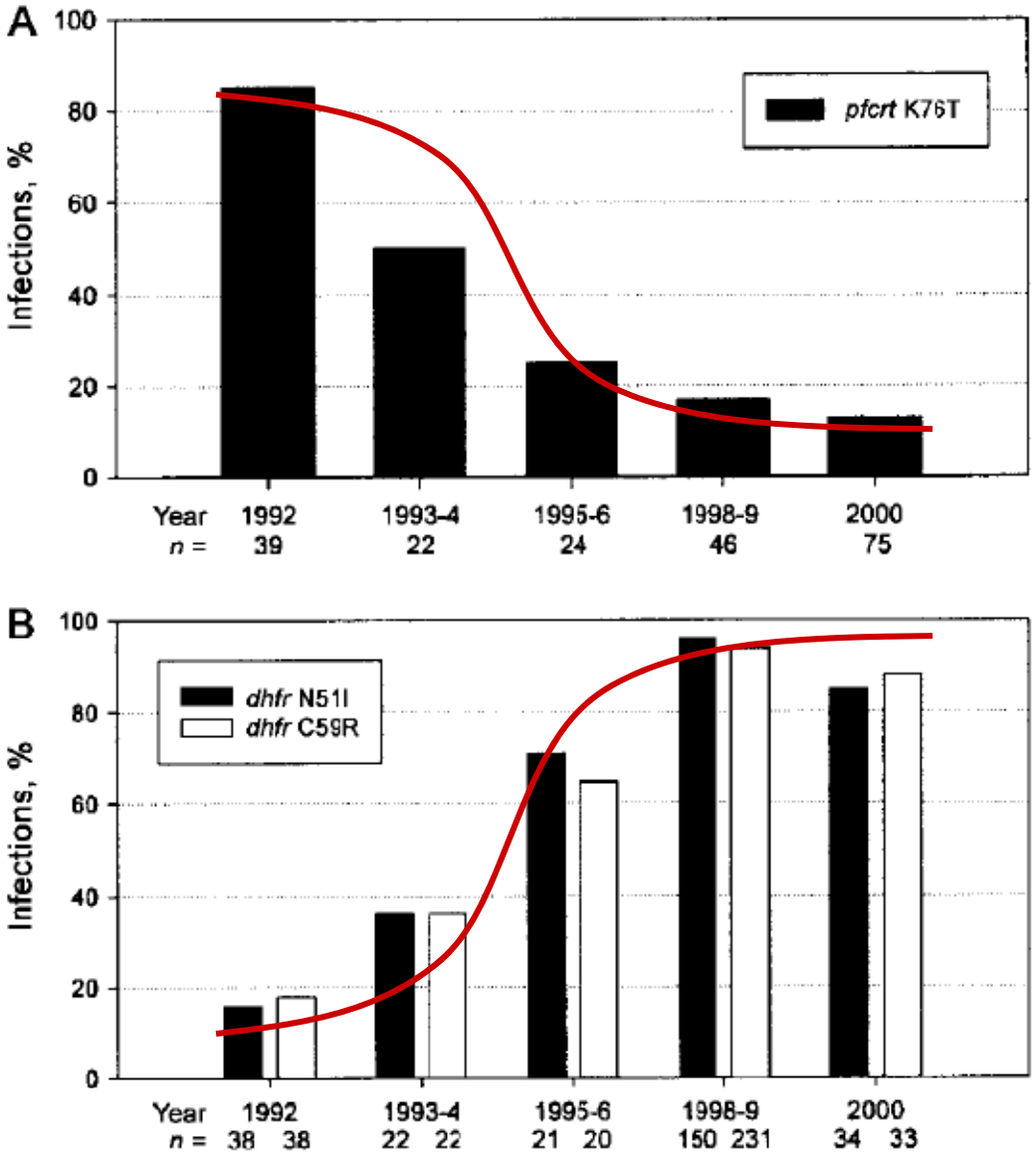
$$+ (1 - \zeta)\, \tau_S \sum_{\mathcal{U}} \delta_{(\mathcal{U} \subseteq \mathcal{R})} \cdot C_{\mathcal{U},\mathcal{R},0}$$

$$\dot{A}_{\mathcal{R},1} = (1 - \varepsilon_1)\, h_{\mathcal{R}}\, S_1 - (\gamma_1 + \nu_{|\mathcal{R}|}) A_{\mathcal{R},1} + g_1 A_{\mathcal{R},0}$$

$$+ \tau_S \sum_{\mathcal{U}} \delta_{(\mathcal{U} \subseteq \mathcal{R})} \cdot C_{\mathcal{U},\mathcal{R},1} + \zeta \cdot \tau_S \sum_{\mathcal{U}} \delta_{(\mathcal{U} \subseteq \mathcal{R})} \cdot C_{\mathcal{U},\mathcal{R},0}$$

$$\dot{C}_{\mathcal{T},\mathcal{R},i} = \xi_{\mathcal{T}} (\varepsilon_i\, h_{\mathcal{R}}\, S_i - \gamma_i A_{\mathcal{R},i}) - [\delta_{(\mathcal{T} \subseteq \mathcal{R})} \cdot \tau_S + \delta_{(\mathcal{T} \subsetneq \mathcal{R})} \cdot \tau_F] \cdot C$$

$$+ \tau_F \cdot \sum_{\{\mathcal{Q} \subset \mathcal{R}:\, \mathcal{T} \cup \mathcal{Q} = \mathcal{R}\}} \sigma_{(|\mathcal{R}| - |\mathcal{Q}|)} \cdot C_{\mathcal{T},\mathcal{Q},i}$$

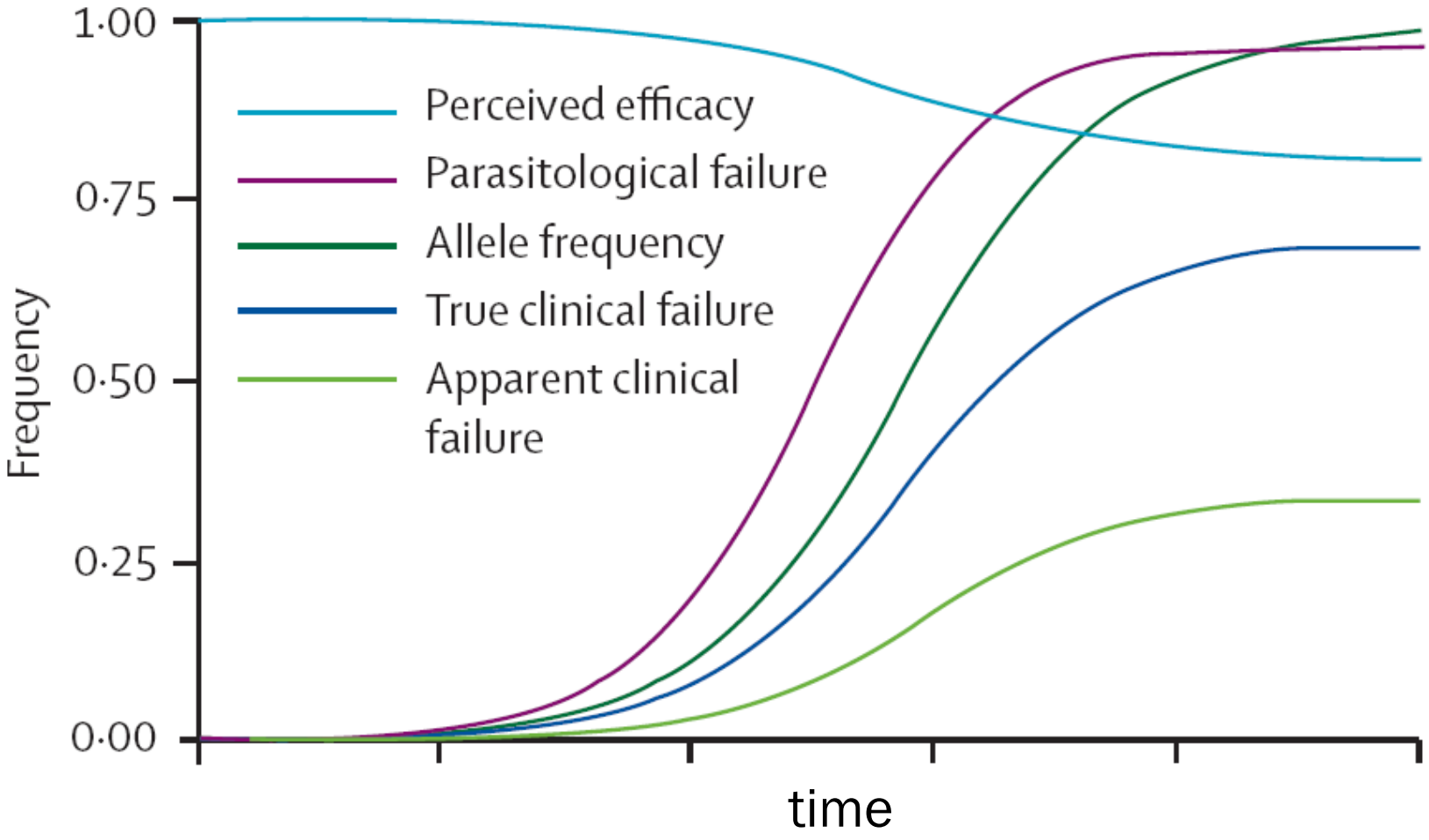


Kublin et al (2003)

Important Parameters

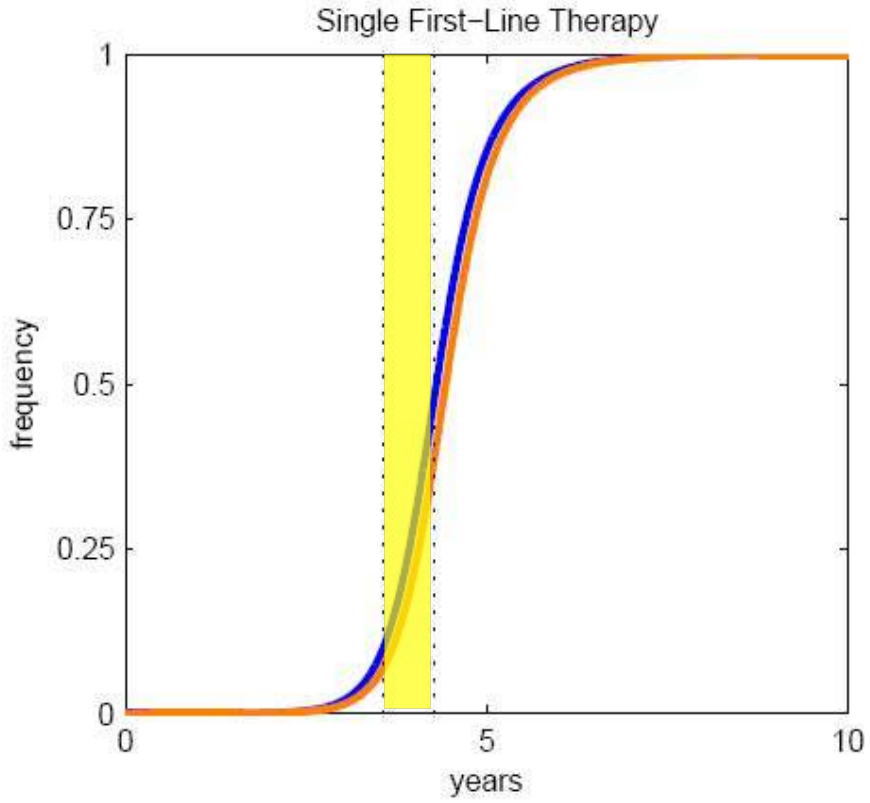
1. fraction of cases treated
2. biological cost of resistance
3. length of evaluation period
4. EIR
5. inbreeding coefficient

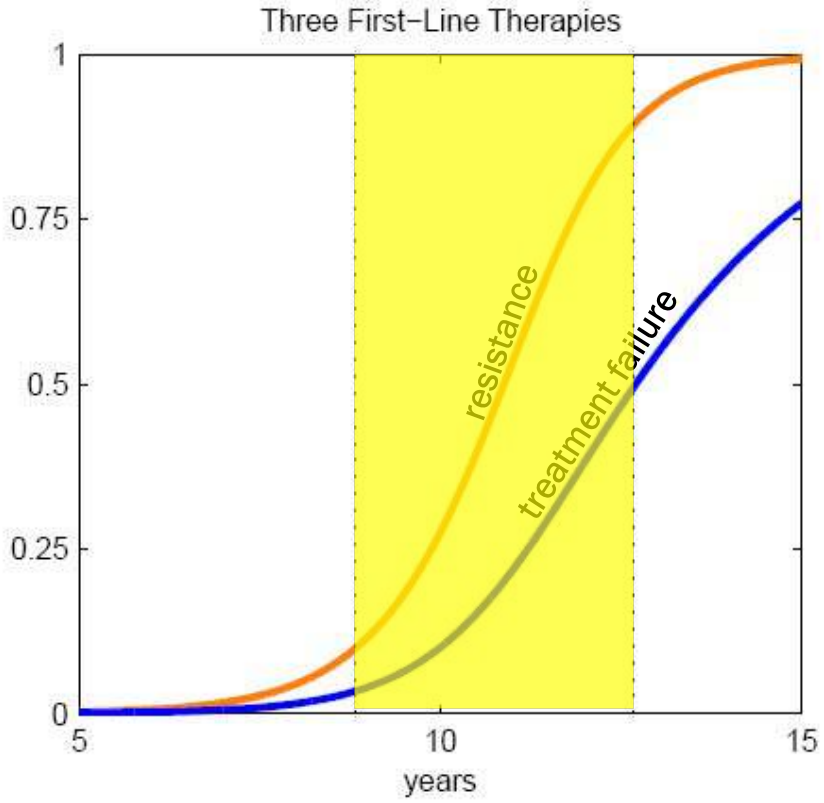
Surveillance



Hastings et al (2007)

Surveillance





Thanks

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