Appendix II, Example II-C

Anti-HIV Clinical Trials

Comparison of Two Drug Combination Clinical Trials

- **AZT + 3-TC and**
- **AZT + Interferon Alpha**

See also: Chou,TC. Integrative Biol. 3: 548-559, 2011 (P.557-558)

Tales of Two Anti-HIV Clinical Trials

	AZT + 3TC	AZT + INF_{α}
Authors	J.J. Eron et al. (9 authors + Northern Am. HIV Working Party	D. Mildvan et al. (21 authors)
Publication	N. Engl. J. Med. 333: 1662-1669, 1995	Antiviral Therapy 1(2): 77-88, 1996
Journal Impact Factor	**28.5**	**3.1**
Number of Patients	**366**	**36**
Surrogate Marker	CD_4^+ , HIV-RNA	P24 Antigen, CD_4^+
Treatment Design	Fractionated Repeated Doses AZT Single Dose, 3TC 2 Doses	Fractionated Repeated Doses Both Drug have 3 Doses
What They Have Proved	"Combination Effect is Greater than Each Drug Alone" Not Possible to Claim Synergism A+B > A, A+B > B ($p<0.001$) (About 5 Yrs Trial)	"Quantitative Determination of Synergism Using Combination Index Method" (CI < 1 indicate synergism) Use Chou-Talalay Method. Adv. Enz. Regul. 22: 27-55, 1984

Conclusion: Synergy is Not determined by p values but rather with the CI values
Synergy is Not a Statistical Issue but rather a Mass-Action Law Issue