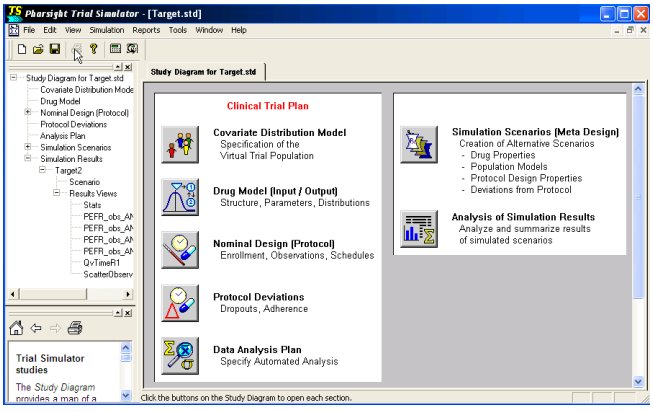
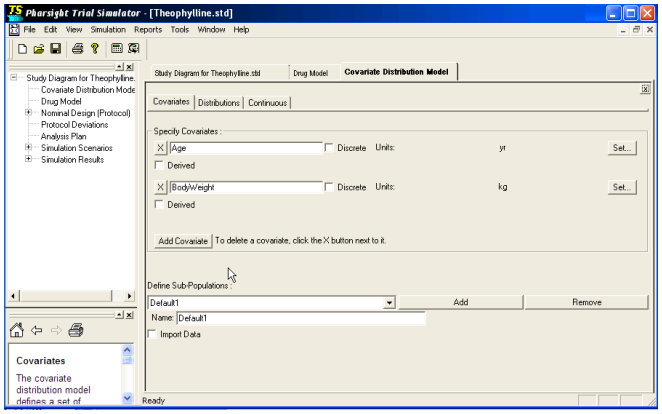
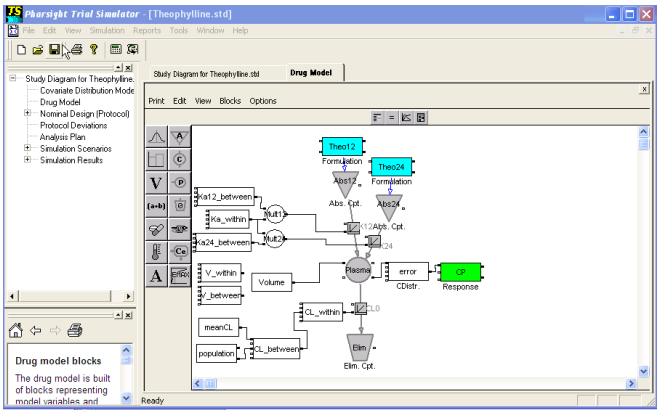
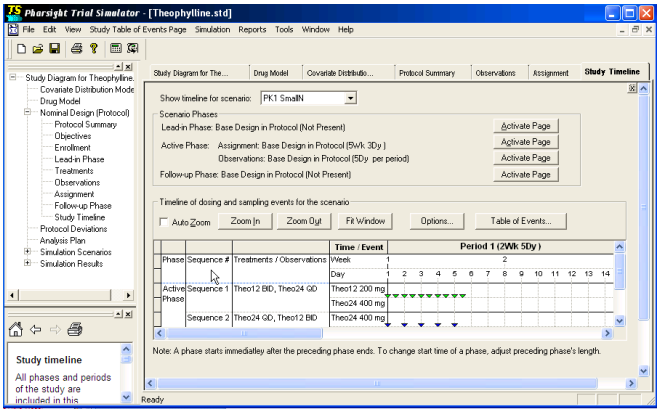
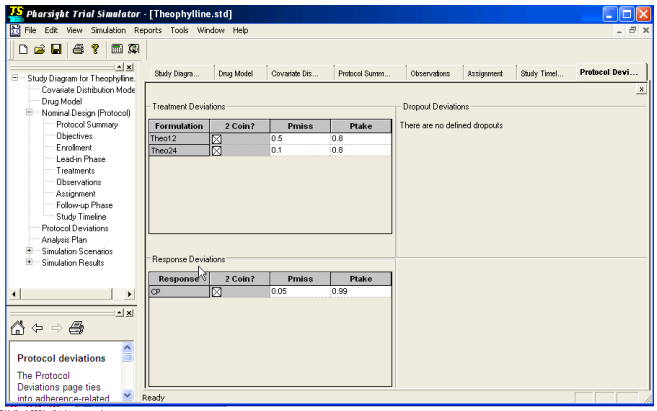
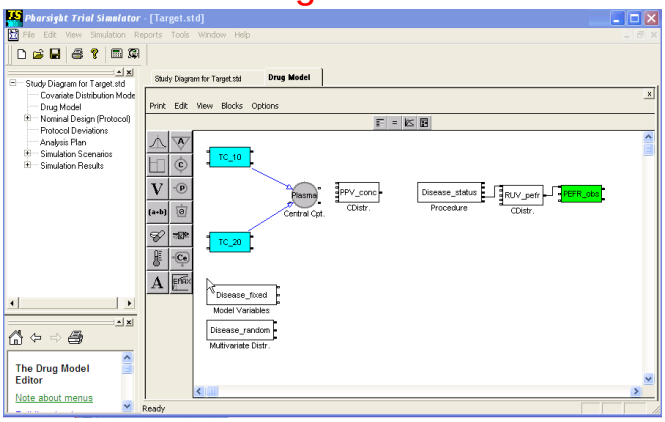
Slide 1	# Clinical Trial Simulation ## Pharsight Trial Simulator Nick Holford Dept Pharmacology & Clinical Pharmacology University of Auckland, New Zealand 		
Slide 2	# Who Started This?  Camilla (Maruszewski) Olson Creative Director at Camilla Olson LLC San Francisco Bay Area | Apparel & Fashion Camilla Olson NOW, thru next Friday, we are holding a sample sale, 50% off pricing. This includes Spring and Fall 2011. We have beautiful items in s 2 - 14, in our proprietary silks, fine wool, and solid silks. These and our priced scarves are available at the studio,... more e (2) • Comment • Send a message • Share • See all activity • 3 days ago Current Creative Director at Camilla Olson LLC Past Intern at Sara Shepherd Community Volunteer at Palo Alto VP Marketing, Founder at Camitro Corporation VP Marketing, Founder at Pharsight Corporation "You are too kind; but you got the history correct. I'll bet your audience cracks up. Who is your audience?" 29 Jan 2012 		http://www.linkedin.com/in/camillaolson 29 Jan 2012
Slide 3	# History of Pharsight • Pharsoft founded by Camilla Olsen in early1996 – Name still used by Pharsight (Jan 2012) Pharsoft Corporation 125 University Ave, Palo Alto, CA 94301 p: 732 280 1480 http://www.pharsight.com • Idea proposed by Carl Peck to Camilla Olsen when attempts to commercialize NONMEM with Beal & Sheiner fell through • Pharsight "Trial Designer" was originally based on a simulation engine licensed from the Right Dose First Time (RIDO) project which was developed at the University of Auckland (Nick Holford) 		

Slide 4	# Amazing Marketing **Trial Design** **Pharsight Trial Designer,** requirements: pentium 90, 33 MB, SVGA monitor with 800 × 600 pixels and 256 colors, CD-ROM drive (required for installation), 32-bit Windows operating systems (Windows 95, 98, NT 3.51, or 4.0), 16 MB RAM for 95, 20 MB for NT 3.51, and 32 for NT 4.0, Microsoft Visual C++ (4.2 for NT 3.51 or 5.0 for NT 4.0 or 95) to create user-defined model components and to link to SAS, PC SAS version 6.12 or later installed as an OLE automation server; $7500, special educational pricing available; Mountain View, Calif, Pharsight Corp, 888-708-7444, info@pharsight.com. *INTRODUCTION*: DRUG DEVELOPMENT IS BIGger and bigger business. The average cost of a compound is now $300 million, and the clinical trials to get the drug ap- *Discussion:* This is not a program to open nonchalantly. It requires a change of mindset and a commitment to learn. Are two days worth the investment in planning a better study? For small studies, perhaps not, but for large studies, and, perhaps more importantly, for a sequence of studies, this sort of structured thinking can only improve the quality of studies. It does not replace the need for a statistician to help decide which design is appropriate. There is no intelligent help to aid you in deciding which design is needed for which phase of the research program. JAMA, March 10, 1999—Vol 281, No. 10 **955** ©NHG Holford, 2004, all rights reserved.	Lehmann HP. Pharsight Trial Designer. JAMA: The Journal of the American Medical Association. 1999;281(10):955-7.
Slide 5	# A Key Insight from Lewis Sheiner ## More than One Model! • Covariate Distribution Model – Distribution of age, sex, renal function, etc. – Create simulated “individuals” • Input-Output (‘Drug Model’) – Mechanistic (PKPD) preferred – Individual and Observation stochastic elements • Nominal Protocol Model – The ideal world – Patients, treatments, observations • Trial Execution Model – Compliance, dropouts, missing samples – Costs ©NHG Holford, 2004, all rights reserved.	Holford NHG, Hale M, Ko HC, Steimer J-L, Sheiner LB, Peck CC. Simulation in Drug Development: Good Practices. http://bts.ucsf.edu/cdds/research/sddgpreport.php. Last accessed 29 January 2012. 1999. .
Slide 6	# What is the Trial Simulator?  ©NHG Holford, 2004, all rights reserved.	

Slide 7	# The Covariate Model  	
Slide 8	# The Drug Model  	
Slide 9	# The Nominal Design Model  	

Slide 10	# The Protocol Deviation Model 	
Slide 11	# Target Concentration Controlled Trial Drug Model 	Holford N, Black P, Couch R, Kennedy J, Briant R. Theophylline target concentration in severe airways obstruction - 10 or 20 mg/L? A randomised concentration-controlled trial. Clin Pharmacokinet. 1993A;25(6):495-505. Holford N, Hashimoto Y, Sheiner LB. Time and theophylline concentration help explain the recovery of peak flow following acute airways obstruction. Population analysis of a randomised concentration controlled trial. Clin Pharmacokinet. 1993B;25(6):506-15.
Slide 12	# Target Concentration Controlled Trial Nominal Design Model