Three Techniques for Rigorous Analysis of Intensive Within-person Experiments

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Thanks to Thomas Pineo, Kay Chen, Katya Hill

Outline

* Thorough clinical research requires intensive, idiographic trials

* Three rigorous analytic techniques

* Three clinical trials using those techniques

Clinician's Dilemma

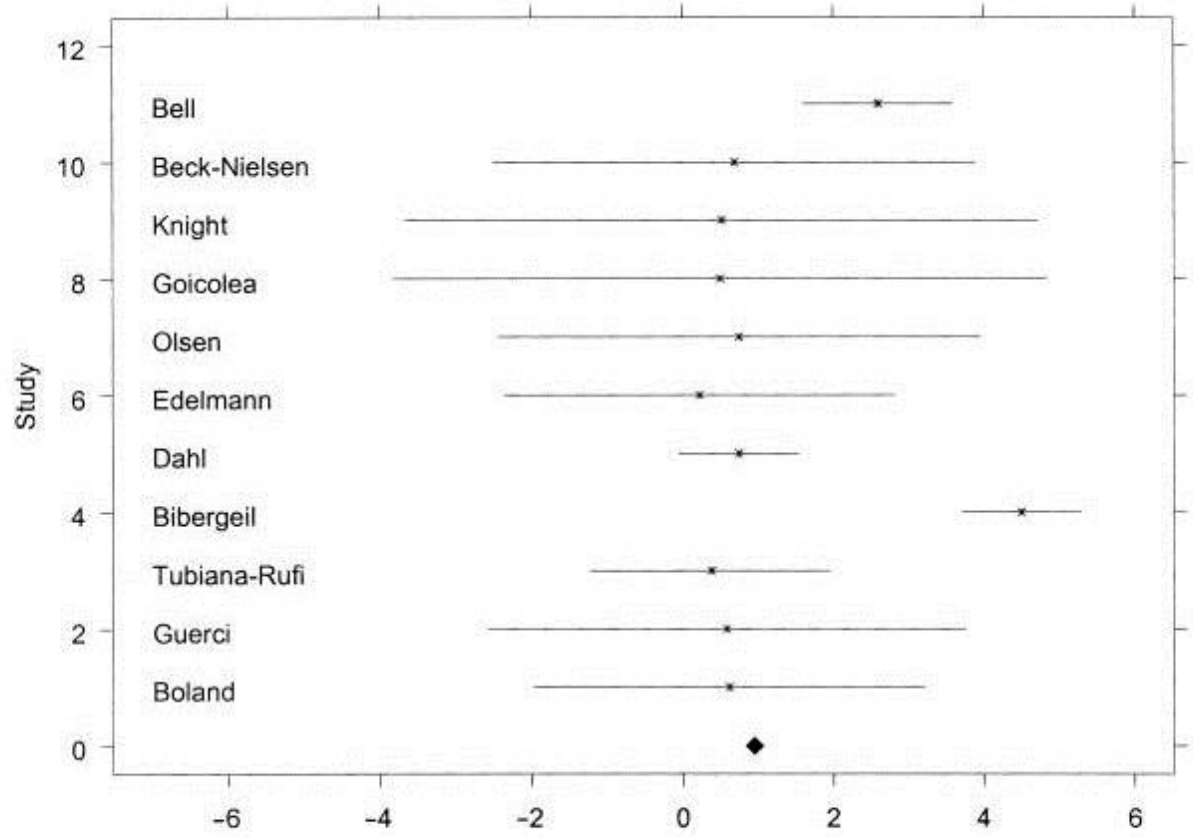
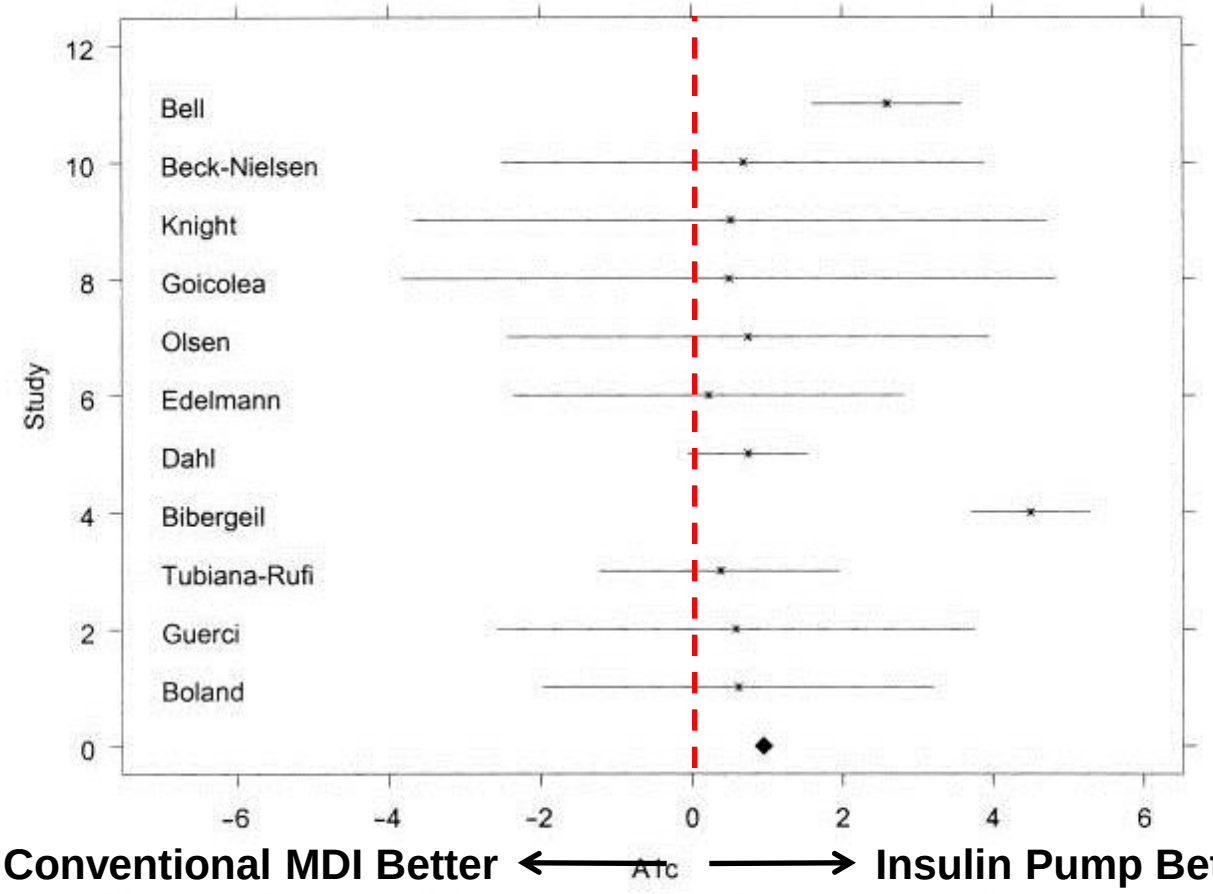


Figure 1—*Effect sizes for parallel design studies. Studies are presented in increasing order of chronology from the bottom, with primary authors' names along the left side of the graph. *Mean effect size. Bars denote the 95% CIs of the mean. Mean effect size for the 11 studies was* d = 0.95.

From: Weissberg-Benchell et al., 03

Clinician's Dilemma



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Needs for Idiographic Clinical Trials

Rare or newly discovered illness

Intervention mechanisms / processes

Small population or available sample

Pilot studies

In-the-field research required

Resolving clinician's dilemma

Quantifying clinician observation

Lack of funding, infrastructure

Patients have study exclusion criteria

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Dr. Thomas Pineo: How to help nursing home residents with diabetes?

Analytic Methods with Promise for Idiographic Clinical Trials

Time Series Analysis

From: Econometrics (Chatfield, 2004)

State-Space Modeling

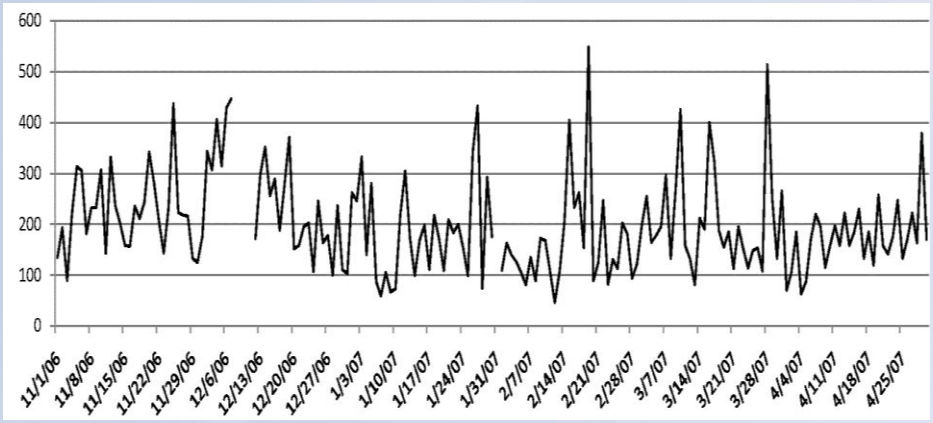
From: Mathematics, Physics (Molenaar, 2003)

Trajectory Analysis

From: Social Sciences (Ridenour et al., 2012)

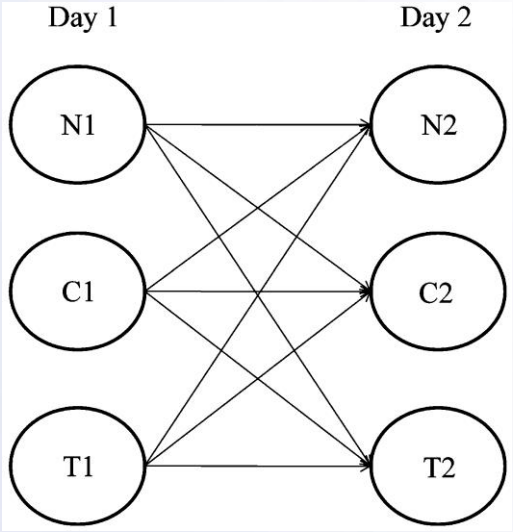
Examples of Models

Time Series Analysis



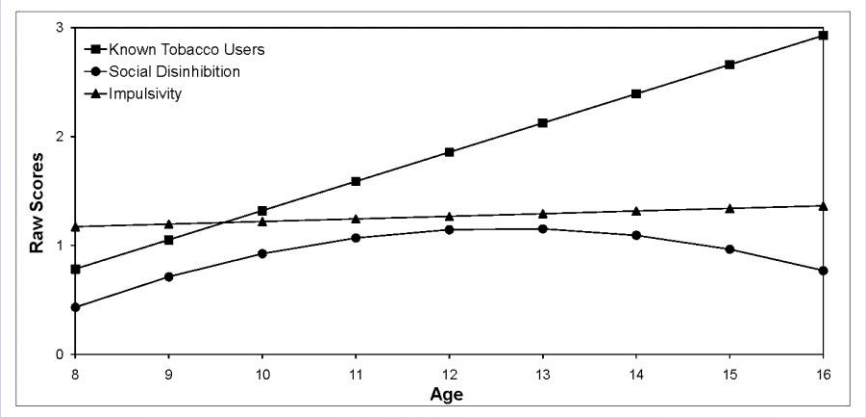
Ridenour et al., 2012

State-Space Models: USEM



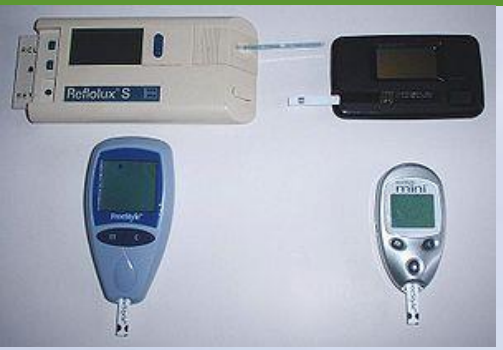
Zheng et al., 2013

Trajectory Analysis



Tarter et al., 2012

Dr. Pineo's Manual Pancreas for Diabetes in Nursing Homes

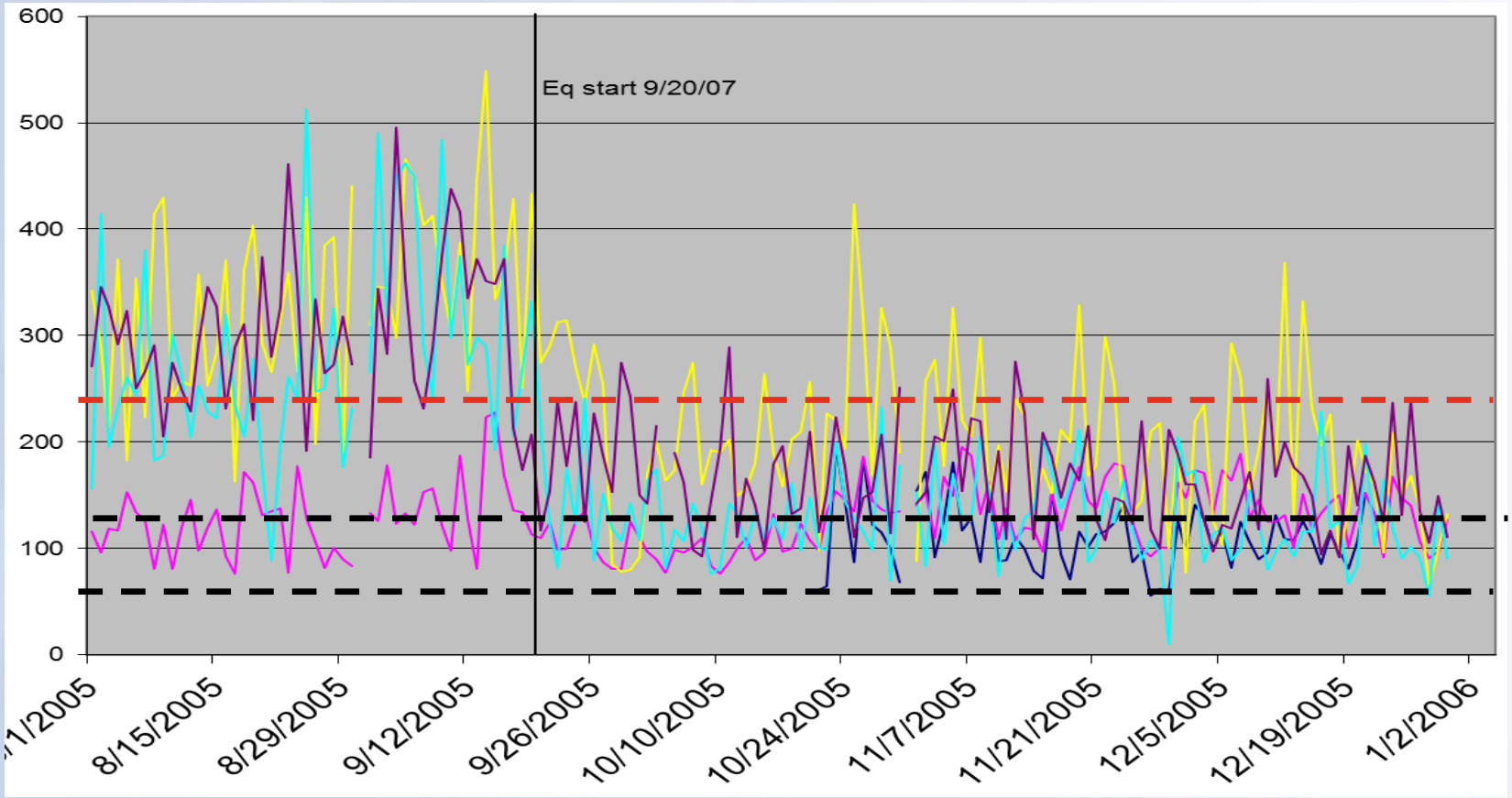


	8/1/05	8/8/05	8/15/05	8/22/05	8/29/05	9/5/05	9/12/05	9/19/05	9/26/05	10/3/05	10/10/05	10/17/05	10/24/05	10/31/05	11/7/05	11/14/05	11/21/05	11/28/05	12/5/05	12/12/05	12/19/05	12/26/05	
Patient A								ss	ss	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	…
Patient B	ss	ss	ss	ss	ss	ss	ss	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	…
Patient C																							…
Patient D																							…

	10/2/06	10/9/06	10/16/06	10/23/06	10/30/06	11/6/06	11/13/06	11/20/06	11/27/06	12/4/06	12/11/06	12/18/06	12/25/06	1/1/07	1/8/07	1/15/07	1/22/07	1/29/07	2/5/07	2/12/07	2/19/07	2/26/07	3/5/07	3/12/07	3/19/07	3/26/07	4/2/07	4/9/07	4/16/07	4/23/07	4/30/07
Patient A	…																													
Patient B	…																													
Patient C	…	ss	ss	ss	ss	ss	ss	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG								
Patient D	…					ss	ss	ss	ss	ss	ss	sG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	GG	G

Ridenour et al., 2013

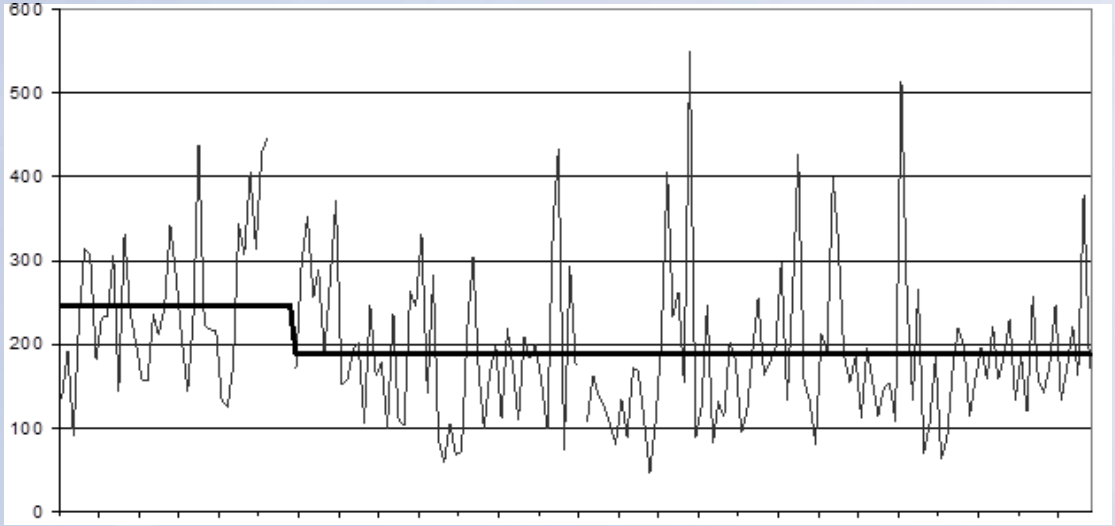
Dr. Pineo's Manual Pancreas for Diabetes in Nursing Homes



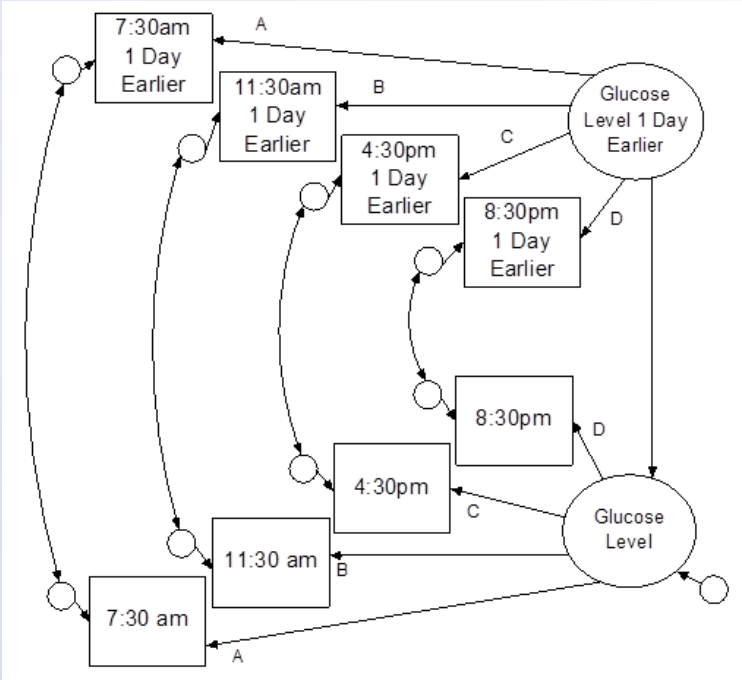
Pineo's Patient B

Dr. Pineo's Manual Pancreas for Diabetes in Nursing Homes

Time Series: ARIMA, Trajectory Analysis



P-Technique



Dr. Pineo's Manual Pancreas for Diabetes in Nursing Homes

	Aggregated Times[A]	7:30am	11:30am	4:30pm	8:30pm	ARIMA
MMTA; Entire Sample	-49.4[a] (9.2)	-35.9[b] (9.8)	-43.3[a*] (194.2)	-59.4[b] (9.7)	-59.1[a*] (277.9)	-52.2 (22.6)
MMTA of Patient A	-40.9[b] (10.7)	0.2[b*] (11.1)	1.8[a*] (24.4)	-50.4[b] (20.2)	-104.2[b] (19.4)	-25.2*
MMTA of Patient B	-107.9[b] (11.8)	-32.2[b] (8.8)	-117.3[a] (23.0)	-156.3[b] (19.3)	-122.2[b] (17.0)	-62.5
MMTA of Patient C	-22.6[b*] (15.3)	11.5 [b*] (27.5)	-66.6[a] (26.8)	-35.5[b*] (25.4)	3.0[b*] (27.7)	-47.9*
MMTA of Patient D	-24.6[b] (10.1)	-112.1[b] (16.0)	26.3[a*] (17.6)	43.5[b] (17.7)	-57.3[b] (24.3)	n/a
P-technique; Entire Sample	-64.9 (6.8)	-32.4 (7.7)	-89.3 (7.6)	-98.8 (6.5)	-83.1 (6.2)	

Note: A = intervention effect aggregated over all times of the day for the sample or specific patient. a = heterogeneous autoregression, lag 2, error covariance structure. b = factor analytic, lag 2, error covariance structure. *Change in glucose was NS (p>.01). Parenthetical values are standard errors. Change attributable to time (slope) and time-intervention interaction were statistically nonsignificant in all MMTA.

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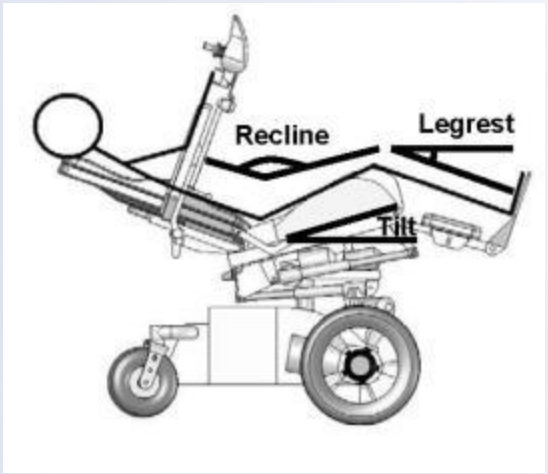
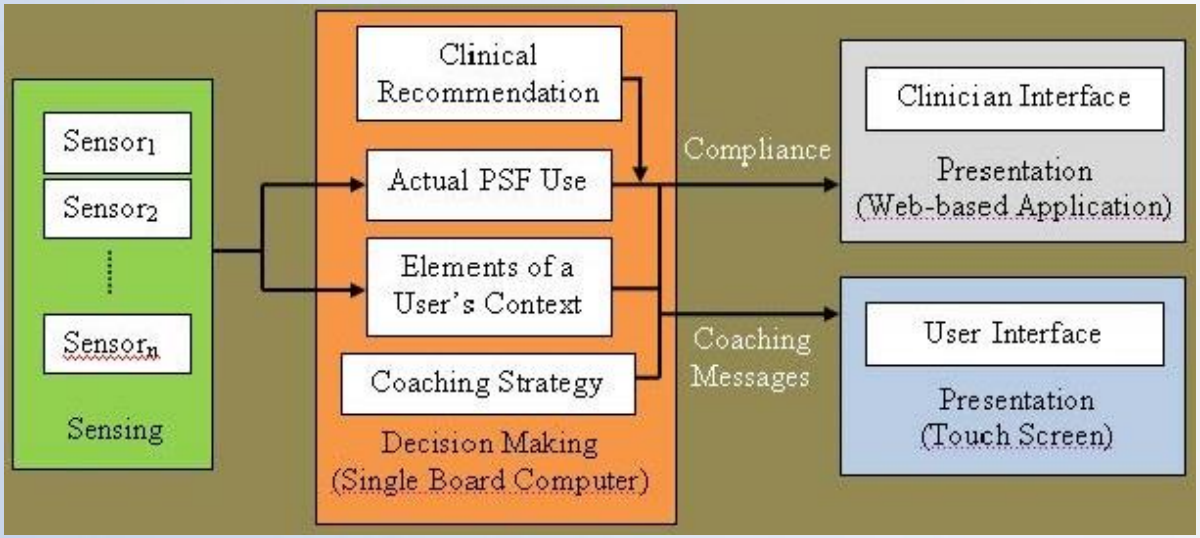
Dr. Pineo's Manual Pancreas for Diabetes in Nursing Homes

	Trajectory Analysis	Time Series / ARIMA	State-space / P-technique
Strengths:	Can model small time series	Models serial dependence	Best reproduction of observed data
	Simplest	Best isolation of efficacy	Easily tests intervention effect on variance
	Most flexible	Can forecast	Mimics large 'N' SEM
	Statistical power		
	Also used with large samples		
Limitations:	Limited serial dependence	Easily made unstable	Easily made unstable
	Coarsest estimate of efficacy	Requires many observations	Requires many observations
			Models are complex

Cooper & Liu's Clinician's Dilemma: Virtual Coach Assistive Technology for Paraplegia





From: Ding et al., 2010

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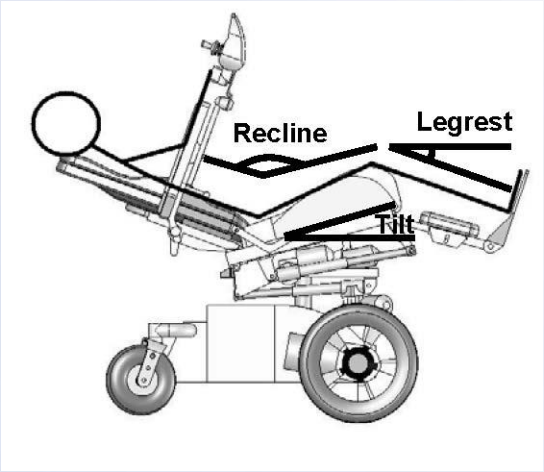

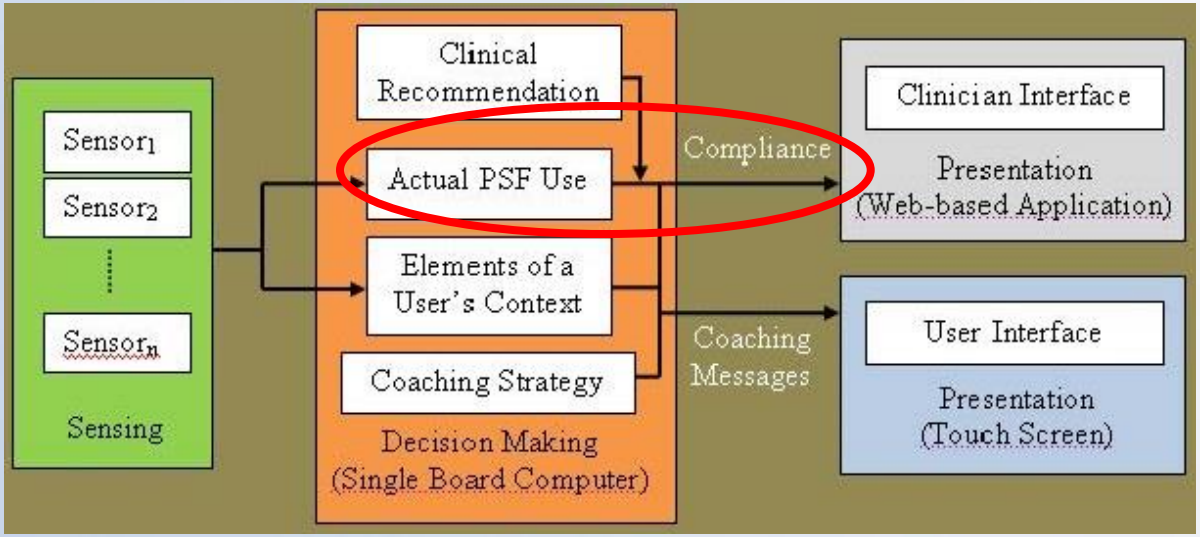

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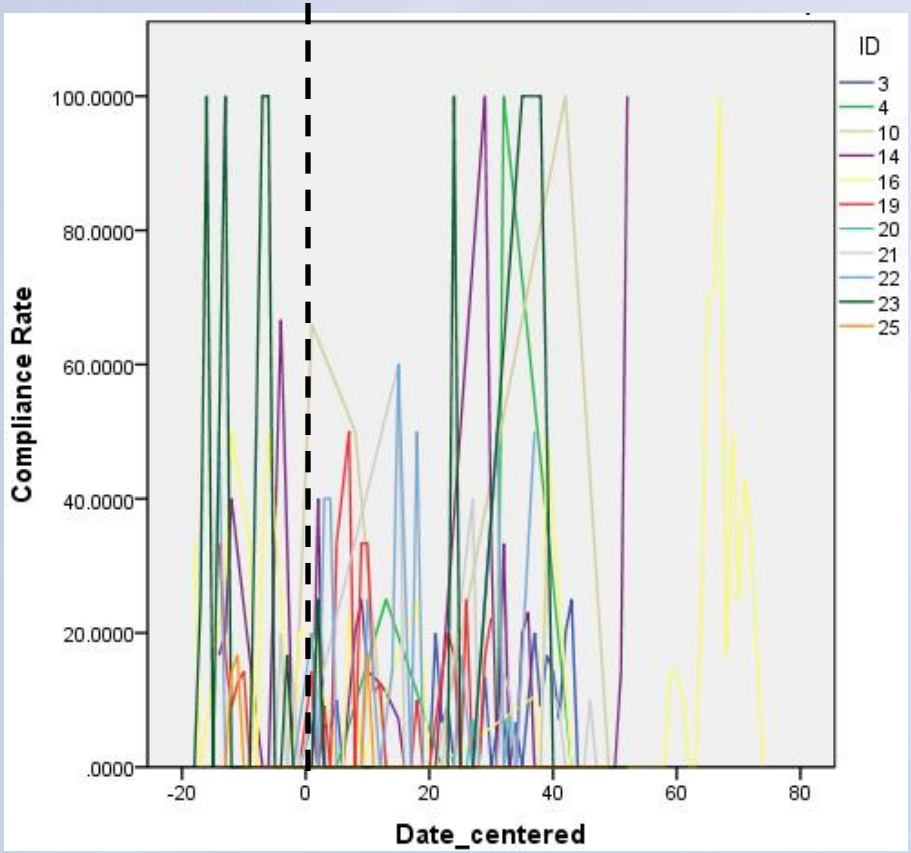
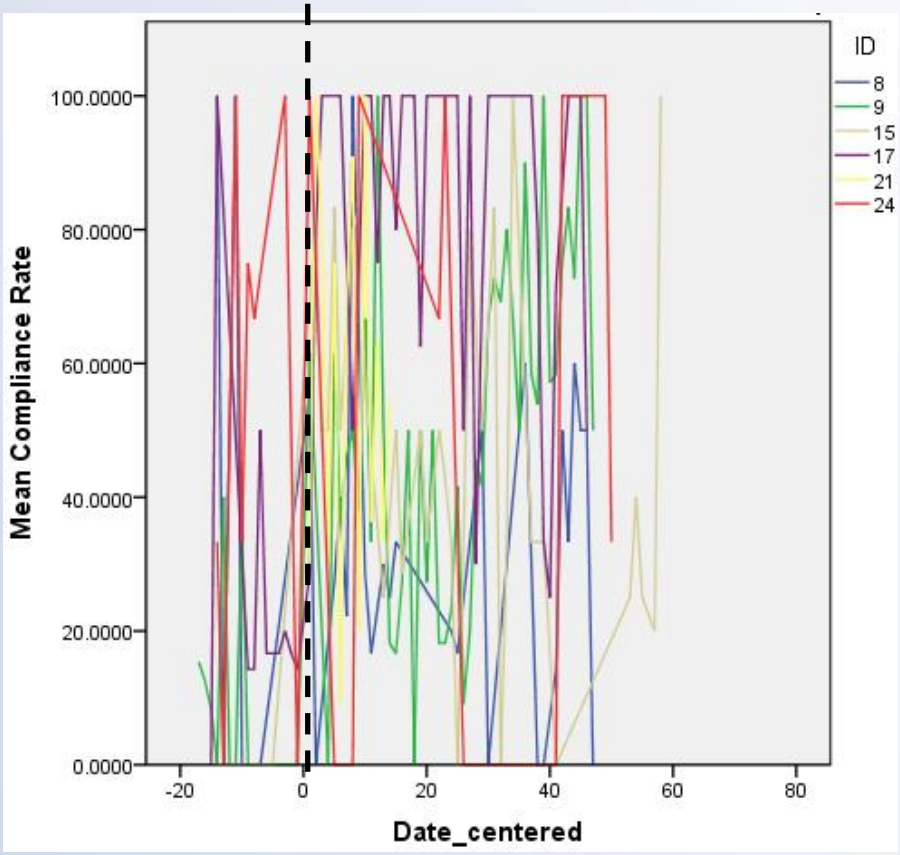
Cooper & Liu's Clinician's Dilemma: Virtual Coach Assistive Technology for Paraplegia

Instruction Only



Instruction + Virtual Coach



Cooper & Liu's Clinician's Dilemma: Virtual Coach Assistive Technology for Paraplegia

	Mean	Standard Deviation	Cohen's d Compared to Baseline
BASELINE (244 observations)			
General Discomfort	41.9	12.39	n/a
Frequency of Use	2.1	2.36	n/a
Duration of Use in Mod/Max 2	50.8	44.78	n/a
Discomfort Intensity	19.2	9.52	n/a
INSTRUCTION (561 observations)			
General Discomfort	42.6	13.01	- -
Frequency of Use[B]	1.5	2.09	0.28
Duration of Use in Mod/Max 2[B]	37.6	46.02	0.29
Discomfort Intensity	19.9	9.36	- -
VIRTUAL COACH (262 observations)			
General Discomfort	42.3	10.81	- -
Frequency of Use[B,I]	3.3	3.02	0.44
Duration of Use in Mod/Max 2[B,I]	67.4	45.73	0.37
Discomfort Intensity[B,I]	10.7	5.52	1.10

Note: [B]Differs from Baseline phase ($p<.001$). [I]Differs from Instruction phase ($p<.001$).

Cooper & Liu's Clinician's Dilemma: Virtual Coach Outcomes

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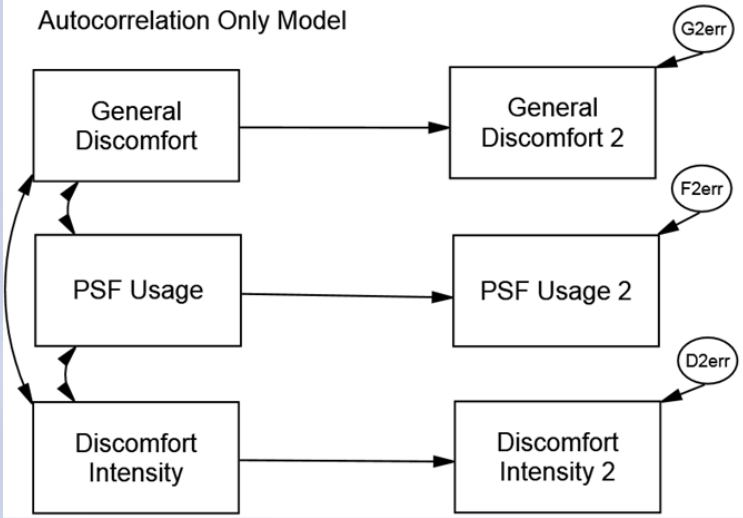
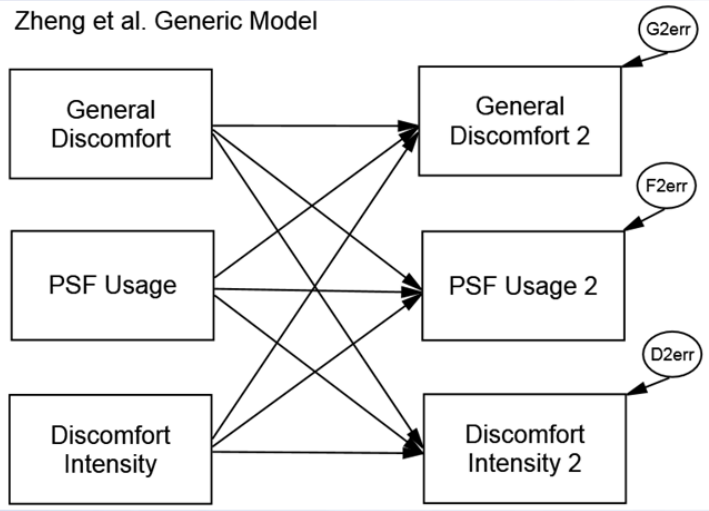
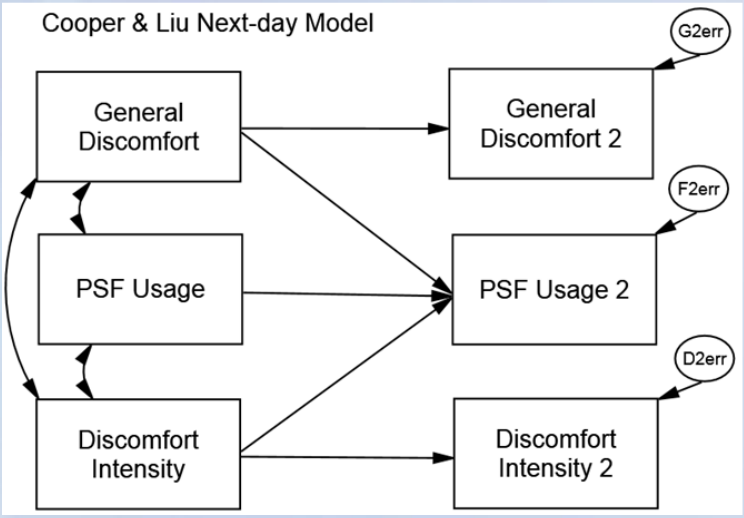
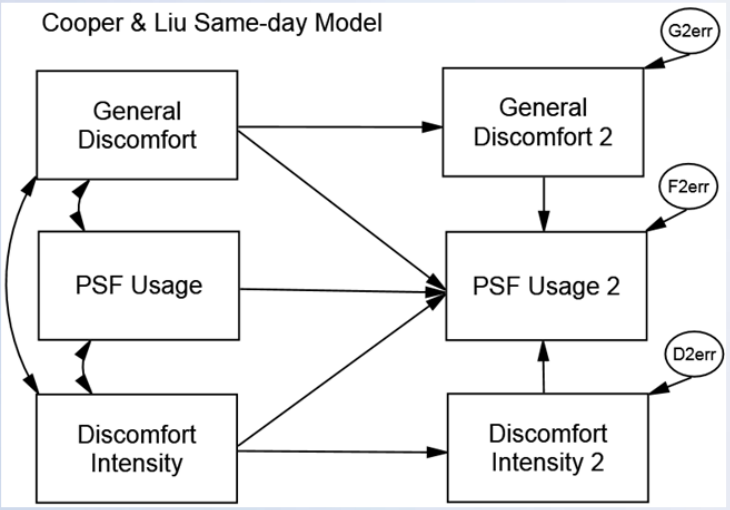
Cooper & Liu's Clinician's Dilemma: Competing Models Relating Discomfort to PSF Usage

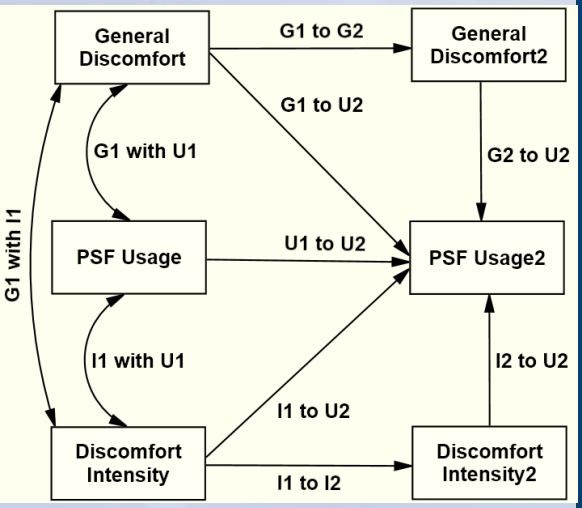








Intervention Process: Discomfort with PSF Usage



Path	Frequency of PSF			Duration of Mod/Max		
	Base-line	Instruct	Virt. Coach	Base-line	Instruct	Virt. Coach
G1 with I1	.69	.37	.67	.67	.39	.66
G1 with U1	.20	.57	.46	.33	.60	.35
I1 with U1	-.04	.22	.56	.12	.12	.35
G1 to G2	.90	.95	.93	.90	.95	.93
U1 to U2	.63	.49	.41	.43	.39	.40
I1 to I2	.92	.92	.91	.92	.92	.91
G1 to U2	.14	.34	.02	.64	.17	.24
I1 to U2	-.08	-.05	.39	-.65	-.33	-.02
G2 to U2	---	---	---	-.32	.26	-.07
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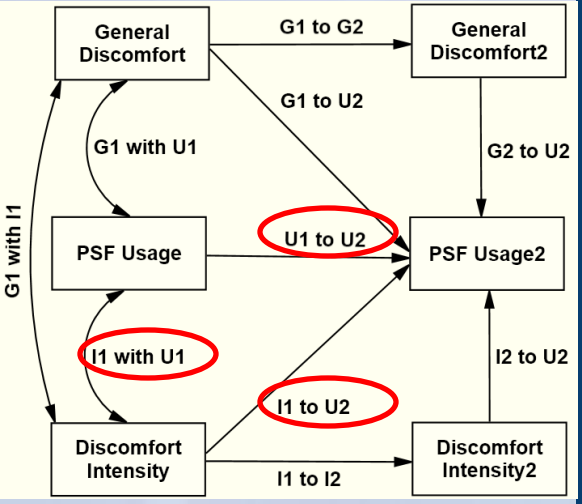

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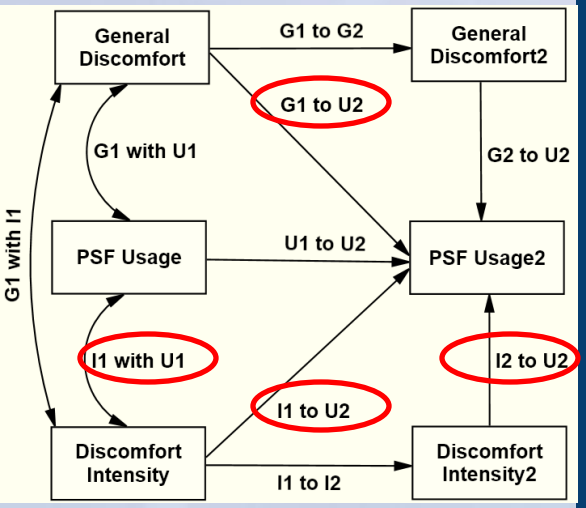

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G2 to U2	---	---	---	-.32	.26	-.07
I2 to U2	---	---	---	**.52**	**.18**	**.12**

Review

* Needs for idiographic clinical trial designs

* Mixed model trajectory analysis
  State-space modeling
  Time series analysis

* Blood sugar, speech acquisition, treatment compliance

Next Steps

* Create tools to support using analytic techniques more widely in idiographic clinical trials

* Numerous specific advances within the particular analytic techniques (e.g., using more complex USEM)

* Demonstrate idiographic clinical trial techniques in a range of fields

References

Chatfield, C. The Analysis of Time Series (6th ed.). Chapman & Hall/CRC, Boca Raton, FL. 2004.

Molenaar, P.C.M. A manifesto on psychology as idiographic science: Brining the person back into scientific psychology, this time forever. Measurement 2004; 2: 201-218.

Molenaar, Peter CM, Richard M. Lerner, and Karl M. Newell, eds. Handbook of developmental systems theory and methodology. Guilford Publications, 2013.

Ridenour, TA, Hall, DL, Bost, JE. A small sample randomized clinical trial methodology using N-of-1 designs and mixed model analysis. American Journal of Drug and Alcohol Abuse 2009; 35: 260-266.

Ridenour TA, Pineo TZ, Maldonado-Molina MM, Hassmiller-Lich, K: Toward idiographic research in prevention science: Demonstration of three techniques for rigorous small sample research. Prevention Science 2013; 14: 267-278.

Sterman, J.D. Business Dynamics: Systems Thinking and Modeling for a Complex World. Irwin McGraw-Hill: Boston, MA. 2000.

Tarter RE, Kirisci L, Ridenour TA, Bogen D. Application of person-centered medicine in addiction. International Journal of Person Centered Medicine 2012; 2: 240-249.