Building More Potent Interventions to Prevent Drug Abuse: Some New Directions

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Building more potent behavioral interventions

- We tend to emphasize establishing whether an intervention has a demonstrable effect
- Equally important is establishing/maximizing how well the intervention works

- A principled approach exists for establishing whether an intervention has a detectable effect – the RCT
- Two emerging principled approaches for building more potent behavioral interventions
  - Experimentation to determine effects of individual intervention components
  - Applying dynamical systems/engineering optimization ideas to intervention development

Approach 1: Experimentation to determine which individual intervention components are active

The idea

- Most interventions are multi-component
- Components are any aspect of an intervention that can be separated out for study, e.g.
  - Normative education, resistance training, homework involving parents, public commitment not to use drugs

The idea

- Obtain a sense of which intervention components are active and which are "dead wood"
  - Retain active components, eliminate others
  - Or… retain any components with effects sizes > some desired level
  - Or… retain components that are worth the resources they require

The idea

- Examination of individual intervention components can be done either…
  - …BEFORE or AFTER a RCT
    - We recommend BEFORE
  - …NONEXPERIMENTALLY or EXPERIMENTALLY
    - We recommend EXPERIMENTALLY
- We recommend a phased experimental approach

Needed: design to isolate individual component effects

- The RCT does NOT provide this isolation
  - Post-hoc analyses do not provide it

- What kinds of designs DO isolate effects?

The beauty of factorial designs

		Component A	
		Off	On
Component B	Off	1 Both off	2 A on, B off
	On	3 A off, B on	4 Both on

- Factorial designs use <u>subjects</u> very efficiently
  - Main effect of Component A: (2+4) – (1+3)
  - Main effect of Component B: (3+4) – (1+2)
  - EACH EFFECT USES ALL SUBJECTS

The beauty of factorial designs

- What if you had 6 intervention components?
- Factorial = 64 conditions
- **Fractional factorial**
  - Factorial in which only carefully selected conditions run
  - Can be best of both worlds

More about fractional factorial designs

- Relatively new to the behavioral sciences
  - Very common in engineering
- The choice of which cells to include is based on key working assumptions
  - Based on theory, prior research, pilot data, etc.
  - Usually concern interactions
    - For example: assume 6-way interaction is effectively zero
- Can be very efficient when many components

Can fractional factorial designs be used in cluster-randomized trials?

- Drug abuse prevention often school-based
- Engineers don’t do cluster-randomized trials
- We have been investigating whether there could be sufficient power

Can fractional factorial designs be used in cluster-randomized trials?

- Suppose 8 intervention components
    - Complete factorial = 256 conditions
- Fractional factorial with 16 conditions provides estimates of 8 main effects and some interactions
- We investigated power, used a simulation to vary
    - Effect size (at the individual level): small (d=.2) or medium (d=.5)
    - Intraclass correlation small (ρ=.01) or large (ρ=.10)
    - Number clusters: 16 or 32
    - Per cluster n: 20, 50, or 300
        - All included a pretest

Scenarios with α=.05, power > .8

Suppose you have *n*=20/cluster.

If ρ=.01 OR ρ=.10:

With **16 clusters** you can detect **medium** effects

(overall *N*=320)

With **32 clusters** you can detect **small** effects

(overall *N*=640)

Scenarios with α=.05, power > .8

Suppose you have $n \geq 50$/cluster

If ρ=.01:

With **16 clusters** you can detect **small** effects

(overall $N \geq 800$)

If ρ=.10:

With **16 clusters** you can detect **medium** effects

With **32 clusters** you can detect **small** effects

(overall $N \geq 1600$)

- These results are preliminary, but…
- … they suggest that individual effects of 8 intervention components can be examined with AS FEW AS16 CLUSTERS to randomize
- More work is needed

Approach 2: Model intervention as a dynamical system, apply optimization procedures from engineering

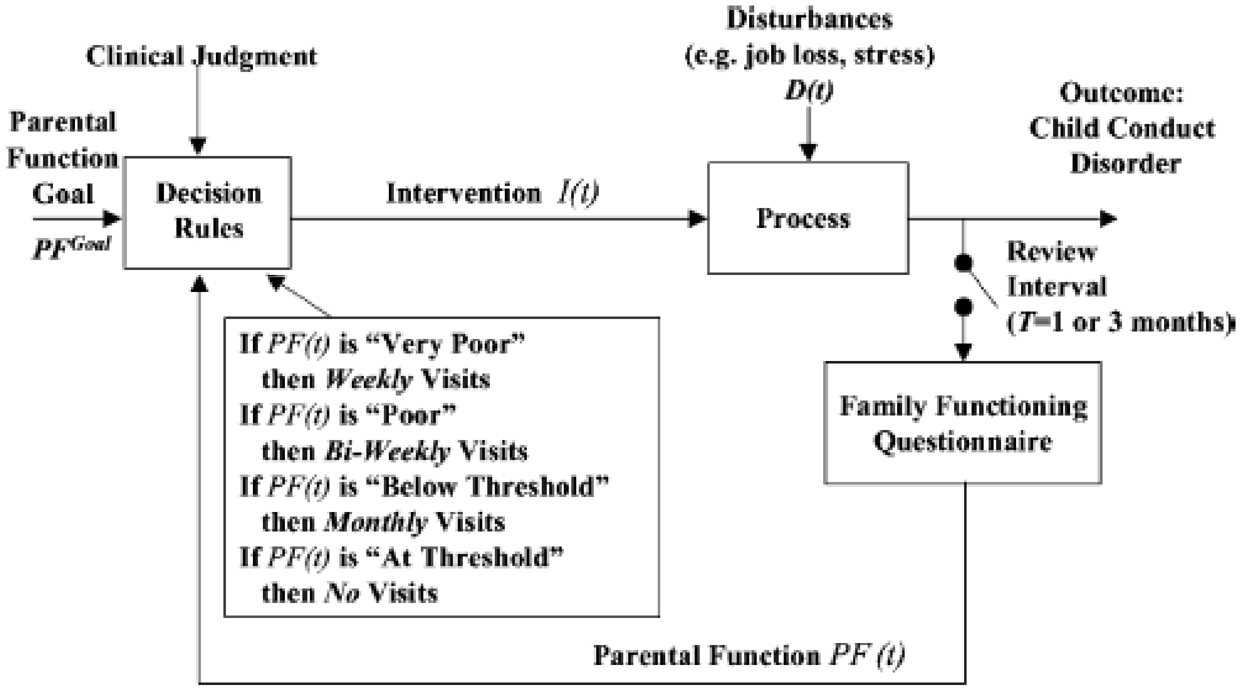
The idea

- Express intervention, including context, as a dynamical model
- Could be a heuristic, could be data-based
- Enables
  - Trying out complicated hypothetical situations
  - Application of engineering optimization procedures

A hypothetical intervention

- Family counseling to prevent conduct disorder in high-risk youth
- Goal is to bring family functioning up to a specified threshold level
- Dose of intervention (number counseling visits/month) is based on
  - Score on family functioning measure
  - Clinical judgment
- Families reassessed periodically, dose may change in response
- Thus this is a time-varying <u>adaptive intervention</u>

The intervention through the eyes of an engineer



From Rivera, Pew, & Collins (2007)

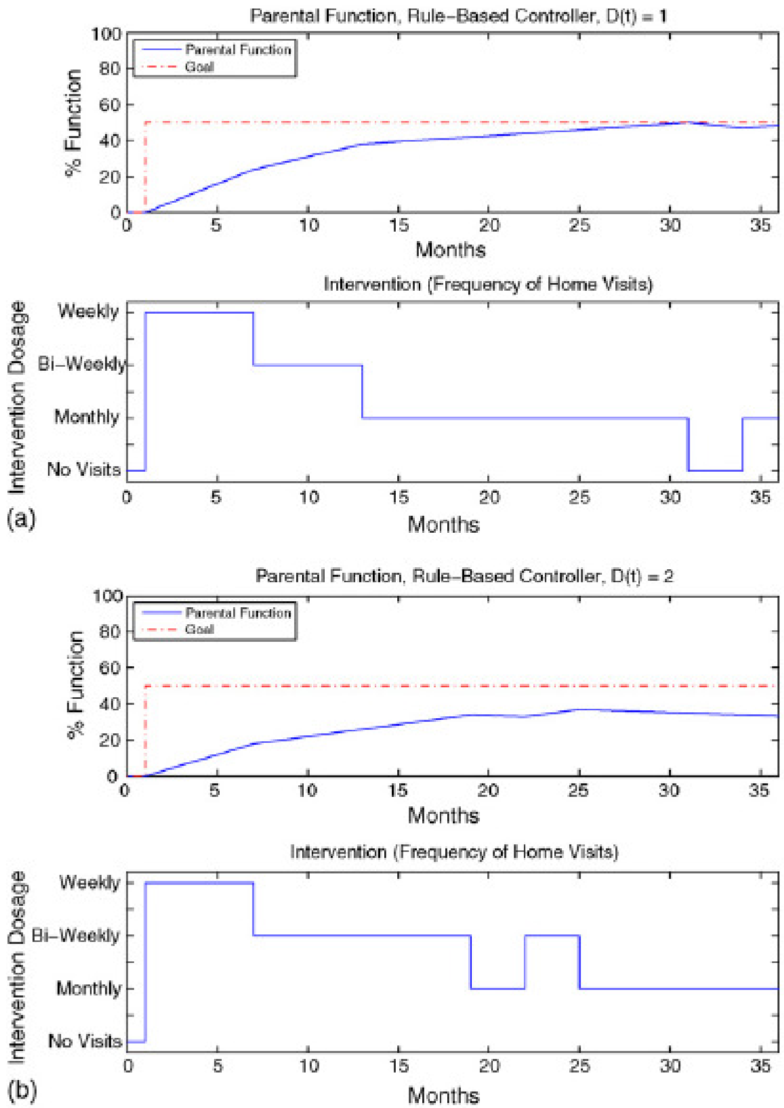


Fig. 6. Simulated closed-loop response of the decision rules of Section 3.3.2 for a family with low intervention gain under both low (a) and high (b) depletion rates $D(t)$. Review interval is quarterly.

From Rivera, Pew, & Collins (2007)

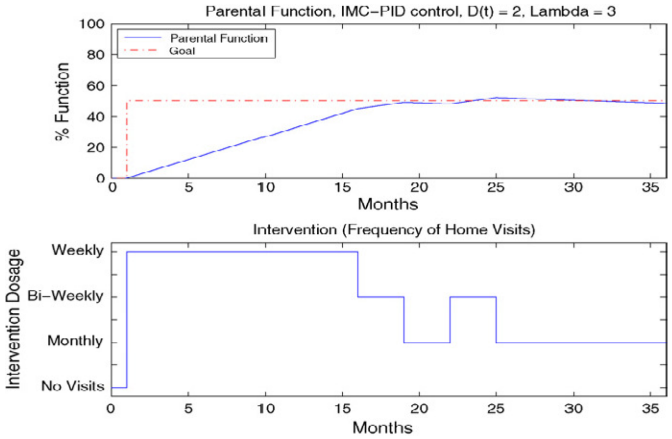


Fig. 8. Simulated closed-loop response of the engineering-based Proportional-Integral-Derivative (PID) control law tuned for the case of a family with low intervention gain under high depletion rate; the review interval is quarterly. The engineering-based decision rule eliminates the offset problem facing the decision rules of Section 3.3.2 under these same conditions by recommending the highest dosage over a longer period of time.

From Rivera, Pew, & Collins (2007)

Engineering-based optimization of interventions

- At this point, a concept
- Work needs to be done on obtaining information needed to model dynamical system
- We are beginning research on this

Engineering-based optimization of multi-level interventions

- It is no problem to include multilevel data structures in dynamical system models
  - And use this in optimizing a single level
- But multilevel *optimization* is not straightforward
  - Trade-offs between optimizing different levels
- In engineering, an active research area

Conclusions

- It is not necessary to settle for simply knowing whether a prevention program has an effect
- Approaches are emerging that will enable prevention scientists to
  - Select only active intervention components
  - Select components and levels that maximize cost-effectiveness
  - Apply optimization procedures
- And thereby develop more potent interventions!

For further information:

- Collins, L.M., Dziak, J.R., & Li, R. (Under review). Choosing among complete factorial, fractional factorial and other designs to maximize scientific gain in relation to resources expended.
- Collins, L.M., Murphy, S.A., & Bierman, K. (2004). A conceptual framework for adaptive preventive interventions. *Prevention Science, 3*, 185-196.
- Collins, L.M., Murphy, S.A., Nair, V., & Strecher, V. (2005). A strategy for optimizing and evaluating behavioral interventions. *Annals of Behavioral Medicine*, *30,* 65-73.
- Collins, L.M., Murphy, S.A., & Strecher, V. (2007). The Multiphase Optimization Strategy (MOST) and the Sequential Multiple Assignment Randomized Trial (SMART): New methods for more potent e-health interventions. *American Journal of Preventive Medicine, 32,* S112-S118 *.*
- Rivera, D.E., Pew, M.D., & Collins, L.M. (2007). Using engineering control principles to inform the design of adaptive interventions. *Drug and Alcohol Dependence, 88,* S31-S40.

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Efficiency in design

- Can refer to
  - number of experimental subjects
  - number of conditions

Comparison of efficiency

- 6 two-level factors
- Want each main effect estimate based on *n*=320

Design approach	Number conditions needed	Number subjects needed	Interaction effects?

Comparison of efficiency

- 6 two-level factors
- Want each main effect estimate based on n=320

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One at a time (6 studies)	12	1920	None

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Design approach	Number conditions needed	Number subjects needed	Interaction effects?
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Single factor	7	1120	None
Complete factorial	64	320	All
Fractional factorial	8-32 depends on design chosen	320	Selected

A hypothetical intervention

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Is this hypothetical intervention multi-level?

- YES in one sense: involves child and child's family

- NO in another sense: child is the only unit of analysis or optimization

Aspects of an intervention in engineering control terms

- From Rivera, Pew, & Collins (2007)

Table 2
Engineering control variables for the hypothetical *Fast Track* adaptive intervention

Adaptive intervention variable	Engineering control term
Intervention: dose of home visits	Manipulated variable
Goal or threshold on parental function	Setpoint
Extraneous sources depleting parental function	Disturbance input
Tailoring variable: parental function	Controlled variable
Review interval: time between adjustments to intervention dose	Controller sampling time