A New Tool for Rapid-Cycle Comparative Effectiveness Research: The Promise of Orthogonal Design

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Lineup for Today's Presentation

- Dominick Esposito (Mathematica)
- Randy Brown (Mathematica)
- Jelena Zurovac (Mathematica)
- Kieron Dey (Nobi Group)

Discussants

- Jodi Segal (Johns Hopkins)
- David Vanness (University of Wisconsin)

Implications of Orthogonal Design for Comparative Effectiveness Research

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Roadmap

- **Introduction to orthogonal design**
  - **Background**
  - **Assumptions and examples**
- **Ongoing study conducted by Mathematica: Special Needs Plan (SNP) care coordination study**
- **Design considerations and challenges**

Motivation: The Need for New Methods

- **Need comparative effectiveness research**
  - **In real-world settings**
  - **Statistically rigorous**
  - **Generating quick results for “rapid-cycle learning”**
- **Much policy research focuses on studying effectiveness of a broad concept**
  - **But effectiveness is highly influenced by operational details of *how* interventions are provided**
  - **Need to learn best ways to implement many components/facets**
- **Orthogonal designs address all these needs**

Introduction to Orthogonal Design

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What is Orthogonal Design?

- Experimental design that allows a simultaneous estimation of the effects of a number of interventions

- Examples of orthogonal designs
  - Full factorial
  - Fractional factorial
  - Plackett-Burman

- Traditional applications
  - Natural science and agriculture
  - Manufacturing
  - Marketing

Design Details

- **Interventions take on two or more levels (variants)**
- **Experimental units (e.g., care coordinators) are randomly assigned to implement predetermined combinations of variants**
  - **Each experimental unit implements one variant for *each* intervention**
- **There is no control group of subjects who do not receive any intervention**
  - **Variation is in the intensity of interventions**

Preview: Three Interventions in SNP Study

	Intervention	Variants
1	**Frequency of Routine Contacts with Patients**	a) Low-risk patients: at least once every 3 months. High-risk patients: at least once or twice per month. Conduct medication review at least once every 3 months b) Low-risk patients: at least once every 2 months. High-risk patients: at least twice or three times per month. Conduct medication review at least once every 2 months
2	**Fall Risk Screening**	a) Current practice b) Use a screening tool; screen at months 1, 4, and 7
3	**Fall Prevention Referral**	a) Current practice b) Current practice AND send patients a letter

Conditions for Unbiased Estimation

- **Orthogonality: independence between intervention assignments for each care coordinator**
  - For each intervention, half of care coordinators are assigned to variant “a” and half to variant “b”
  - Half of care coordinators assigned to “a” for one intervention are assigned to “a” for another intervention and half to “b”
- **Homogeneity: care coordinators must have similar average outcomes across their case loads at baseline**

Basis for SNP Study Design (Plackett-Burman 12)

	Intervention										
Care Coordinator	1	2	3	4	5	6	7	8	9	10	11
1	a	a	b	a	a	a	b	b	b	a	b
2	b	a	a	b	a	a	a	b	b	b	a
3	a	b	a	a	b	a	a	a	b	b	b
4	b	a	b	a	a	b	a	a	a	b	b
5	b	b	a	b	a	a	b	a	a	a	b
6	b	b	b	a	b	a	a	b	a	a	a
7	a	b	b	b	a	b	a	a	b	a	a
8	a	a	b	b	b	a	b	a	a	b	a
9	a	a	a	b	b	b	a	b	a	a	b
10	b	a	a	a	b	b	b	a	b	a	a
11	a	b	a	a	a	b	b	b	a	b	a
12	b	b	b	b	b	b	b	b	b	b	b

Implications

- **Designs that use few care coordinators relative to the number of interventions tested**
  - **Allow unbiased estimation only of main effects**
  - **Main effects are confounded with two- and higher order interactions**
- **Increasing the number of care coordinators**
  - **Reduces the number of confounding interactions**
  - **Increases the number of interventions that can be tested**
  - **Increases the power to detect impacts**

Comparison of Orthogonal Designs

Type of design	Main effects are unconfounded with one another	Main effects are unconfounded with two-way interactions	Minimum number of care coordinators needed to test 11 interventions
Full Factorial	Yes	Yes	2^{11}= 2,048
Plackett-Burman Resolution III	Yes	No	12
Plackett-Burman Resolution IV	Yes	Yes	24

Estimating Intervention Effects

- Simple estimate of main effects
  - Difference in average outcome between care coordinators that provide one variant (a) and those that provide the other (b)
- Regression analysis
  - Observations can be patient-level or means for care coordinators
  - Regress outcomes on binary indicators for each intervention denoting the assigned variant

SNP Care Coordination Study

- SNPs were established to improve care for high-risk Medicare beneficiaries
- Care coordination programs consist of a wide range of interventions
- Little is known about what works best for whom and under what circumstances
- Differences in intensity and implementation can influence intervention effectiveness (Mahoney 2010)

Background

- **25 care coordinators at two SNPs provide services to 1,500 dually eligible patients with disabilities**
- **11 interventions implemented over 12 months address**
  - **Routine contact with patients**
  - **Screening for fall risk**
  - **Depression screening**
  - **Care plan review**
  - **Patient coaching and engagement**
  - **Follow-up post discharge**

Outcomes and Analysis Strategy

- **Outcomes**
  - **Hospital admissions and readmissions**
  - **Emergency room visits**
- **Analysis strategy**
  - **Estimate main intervention effects**
  - **Regression-adjusted for baseline characteristics:**
    - Pre-intervention value of key outcomes at care coordinator and patient level
    - Demographics (age, race, gender)
    - Chronic conditions

Contacts, Falls and Depression Screening

	Intervention	Variants
1	**Frequency of Routine Contacts with Patients**	a) Low-risk patients: at least once every 3 months. High-risk patients at least once or twice per month. Conduct medication review at least once every 3 months b) Low-risk patients: at least once every 2 months. High-risk patients: at least twice or three times per month. Conduct medication review at least once every 2 months
2	**Fall Risk Screening**	a) Current practice b) Use a screening tool; screen at months 1, 4, and 7
3	**Fall Prevention Referral**	a) Current practice b) Current practice AND send patients a letter
4	**Depression Screening Tools**	a) Use PHQ-2 tool b) Use PHQ-9 tool
5	**Depression Screening Frequency and Referral**	a) Conduct depression screening at least once every 6 months. If patient screens positive, refer the patient for a mental health intervention as per current practice. b) Conduct depression screening at least once every 3 months. If patient screens positive, refer the patient for a mental health intervention as per current practice AND send a letter encouraging mental health follow-up to the primary care provider

Care Planning and Coaching

	Intervention	Variants
6	**Frequency of Care Plan Review**	a) Current practice b) Review care plan at least once every 3 months
7	**Coaching About Health Care Needs**	a) Current practice/clinical judgment b) Use the teach-back method when providing instructions and coaching to patients
8	**Disease Management Education**	a) Current practice b) Provide additional education about disease management for patients with chronic conditions

Care Transitions

	Intervention	Variants
9	**Frequency of Patient Contact After Discharge**	a) Contact patient within three business days post-discharge b) Contact patient within three business days post-discharge AND within seven days of first followup
10	**Communication with Primary Care Provider (PCP) After Discharge**	a) Inform patient's PCP of the patient's discharge through written notification (letter) b) Inform patient's PCP of the discharge through written notification (letter) AND via telephone (voicemail)
11	**Follow-up with Patient After Discharge**	a) Current practice b) Administer CTM-3 instrument and use a structured checklist during follow-up

SNP Study Design (Plackett-Burman 24)

	Intervention										
Care Coordinator	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
1	a	a	b	a	a	a	b	b	b	a	b
2	b	a	a	b	a	a	a	b	b	b	a
3	a	b	a	a	b	a	a	a	b	b	b
4	b	a	b	a	a	b	a	a	a	b	b
5	b	b	a	b	a	a	b	a	a	a	b
6	b	b	b	a	b	a	a	b	a	a	a
7	a	b	b	b	a	b	a	a	b	a	a
8	a	a	b	b	b	a	b	a	a	b	a
9	a	a	a	b	b	b	a	b	a	a	b
10	b	a	a	a	b	b	b	a	b	a	a
11	a	b	a	a	a	b	b	b	a	b	a
12	b	b	b	b	b	b	b	b	b	b	b
13	b	b	a	b	b	b	a	a	a	b	a
14	a	b	b	a	b	b	b	a	a	a	b
15	b	a	b	b	a	b	b	b	a	a	a
16	a	b	a	b	b	a	b	b	b	a	a
17	a	a	b	a	b	b	a	b	b	b	a
18	a	a	a	b	a	b	b	a	b	b	b
19	b	a	a	a	b	a	b	b	a	b	b
20	b	b	a	a	a	b	a	b	b	a	b
21	b	b	b	a	a	a	b	a	b	b	a
22	a	b	b	b	a	a	a	b	a	b	b
23	b	a	b	b	b	a	a	a	b	a	b
24	a	a	a	a	a	a	a	a	a	a	a
25	b	b	a	a	a	b	a	b	b	a	b

Key Study Design Considerations

- Which interventions to test?
  - Do interventions have potential to improve outcomes?
  - Can interventions be implemented without excessive oversight?
  - Are the interventions likely to be adopted, if found effective?
- How many interventions to test?
  - Tradeoff between reducing confounding or testing more interventions
- Is there enough power to detect impacts?
- How long should the trial run?

Challenges

- Same implementation challenges as in any other study, but implementation might appear more overwhelming
- Fidelity to assigned interventions
  - Motivation and skills of implementers
  - Number of interventions tested
- Homogeneity
  - Care coordinators may be assigned heterogeneous case loads or differ in skills and ability

Tools for Successful Implementation

- **Pre-study: Engage implementers in the design and provide timely training and tools**
  - **Implementation guides**
  - **Individualized assignment sheets**
  - **Intervention tracking sheets**
- **Post-study: Assessment of facilitators and barriers to implementation**
  - **Use tracking sheets to examine fidelity to interventions**
  - **Discuss study with implementers**

Conclusion

- **Orthogonal design is a powerful tool that is well suited for comparative effectiveness research because**
  - **It is amenable to testing real-world effectiveness**
  - **It combines the rigor of experimental design with the ability to produce rapid results**
  - **It allows for the direct assessment of whether more resource-intensive interventions yield sufficiently better patient outcomes**
  - **It can be used to assess which intervention variants work best for different patient types**

Implementation of Orthogonal Designs in the Real World

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Implementation Follows Good Design

- **100% implementation success may require declining a percentage of the asks before Day 1**
- **Proof of good design comes when the numbers improve as predicted**
- **Scientist leads discovery of 20+ interventions**
- **Homogeneity (Shewhart limits) and dry-run pre-study are bedrock**
- **Improvement often starts *during* study**
- **Intent-to-treat (in scantness and adherence)**

Implementation Is the Hardest Part

- Post-study discovery *before* showing results
- Overcome objections (e.g., regression-to-the-mean, false-alarms, findings/interactions “not credible”)
- Scientific work to find and fix early implementation problems: the brown bag and CAD examples
- Listen past the people to the process

Riddle

- **Why does false-alarm rate decrease when testing 20+ interventions (and hence false-alarm is problematic in smaller designs)?**
- **Why is this important in implementation?**

How to Perfect Implementation

- Develop method over a few dozen large orthogonal studies
- Combines scientific and management work
- Requires re-study of important literature:
  - E.g., Shewhart (1931), Fisher (1926, 1935), Box and Draper (1966)
- Scientific vs. empirical feedback/control

Final Clues

- Mathematics are to implementation as toes are to walking (i.e., necessary but insufficient)
- Knowing how the thing works at all times and places drives implementation results to predicted level
- "I learned innovation is a very difficult thing in the real world" Richard Feynman (1985)
- Orthogonal design is a top management tool, not implemented top-down (but starts there)
- People implement: they have to be persuaded to take it but will retain the freedom to leave it

Discussants

Jodi Segal, Johns Hopkins University

David Vanness, University of Wisconsin

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Orthogonal Design Resources (1)

- Less technical reads
  - Anderson, Mark, and Patrick Whitcomb. *DOE Simplified: Practical Tools for Effective Experimentation.* Productivity Press, 2007.
  - Ledolter, Johannes, and Arthur Swersey. *Testing 1 - 2 - 3: Experimental Design with Applications in Marketing and Service Operations.* Stanford Business Books, 2007.
- Standard textbook
  - Box, G. E. P., W.G. Hunter, and J.S. Hunter. *Statistics for Experimenters.* New York: Wiley, 1978.

Orthogonal Design Resources (2)

- Statistical foundation
  - Box, G.E.P. and N.R. Draper. Evolutionary Operations. Wiley, 1969.
  - Fisher, R.A. The Arrangement of Field Experiments. *Journal of the Ministry of Agriculture of Great Britain*, vol. 33, 1926, p. 503-513.
  - Fisher, R. A. *The Design of Experiments,* 1st ed. London: Oliver and Boyd, 1935.
  - Plackett, R. L., and J.P. Burman. “The Design of Optimum Multifactor Experiments.” *Biometrika,* vol.33,1946, p. 305.
  - Shewhart, W.A. Economic Control of Quality of Manufactured Product. Van Nostrand, 1931.

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– Mahoney, Jane E. “Why Multifactorial Fall-Prevention Interventions May Not Work: Comment on “Multifactorial Intervention to Reduce Falls in Older People at High Risk of Recurrent Falls.” *Archives of Internal Medicine*, vol. 170, no. 13, 2010, p. 1117.

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Save the date for the next Center on Health Care Effectiveness Forum:

"Implementing the Patient-Centered Medical Home: Remaining Questions and Challenges"

June 7, 2012

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