Adherence Research: Stick to the Past of Jump to the Future?

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Background and Approach

- How did we get to this morning’s session?
- Identifying themes and asking questions
  - No “singling out” - not citing articles as negative or positive examples – unfair to authors and other authors –
  - There are many examples – good and bad
- Foundation for panel discussion
My perspective

• Not an adherence researcher – but long involvement
  • Methodologist
  • Outcomes and (comparative) effectiveness researcher
    • Interventions in the “real world”
    • Individual to systems interventions
    • Patients to populations

• Trained as a psychiatric-mental health nurse
• Translational

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<th>Basic Science Discovery</th>
<th>Early Translation</th>
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- Identification of opportunities and approaches to health problems
- Discovery of candidate health application
- Health application to evidence-based guidelines
- Practice guidelines to health practices
- Practice to population health impact

• Pragmatist

- Applicability
- Replicability
- Scalability
- Affordability
- Sustainability

• Litmus test: “how ready is it for patient care?”
Validate and (hope to) extend

Variations in Patients’ Adherence to Medical Recommendations
A Quantitative Review of 50 Years of Research
M. Robtn DiMatteo, PhD

Many theoretical models (eg, Health Belief Model, Theory of Planned Behavior, and Transtheoretical Model) focus on understanding, predicting, and improving adherence. Their common components involve health professional–patient communication, patients’ cognitive and social processes (eg, beliefs, norms), and patients’ resources (eg, financial, psychologic, and social support). The empirical literature on adherence is large but not well understood, even with elegant conceptual frameworks. Studies vary widely in methodologies, and operational definitions of adherence are as varied as the diseases, regimens, and patients examined. Both measurement and context differences produce wide variations in adherence estimates, correlates, and outcomes.
Nomenclature

- Compliance, adherence, concordance, persistence, medication behavior, patient-centric, intentional/non-intentional, willfully negligent, ...

Back to the ABCs

- Validation?
- “Pressure points”?
- Messaging to the field: consistent use of the term adherence?
- Integrate subclinical nonadherence

Nomenclature

• “Suboptimal adherence”

• “Suboptimal traffic flow”?
Nomenclature

• Severity = “what patient did not do”

• Consequences of non-adherence as marker of severity of non-adherence
  • (Likely) outcome severity = severity of non-adherence
  • Bayesian approach
  • Subclinical non-adherence
Nomenclature

• What have we learned from other areas of behavior change e.g.
  • Smoking cessation
  • Weight loss

• “Relapsing conditions”:
  • Non-adherence as a relapsing condition
Nomenclature

Tower of Babel

• Common data models
  • Determinants
  • Measurement of adherence
  • Outcome

• Reporting standards
  • “CONSORT”-like statement
Psychological aspects

- Is (non-)adherence merely a behavior?

- State vs. trait debate
- Intrinsic vs. extrinsic adherence
- (Non-)adherence as a personal decision
  - a-contextual?
  - driven by personal health experiences?

Non-adherence
Neo-adherence
Adherence
Context

- Predominant focus on the patient-related factors vs. WHO framework:
  - Study each dimension separately?
  - What part of the variance in adherence behavior is attributable to each dimension?
  - Hierarchical approach?
    - What are the “supra-patient” dimensions that influence patient-level behavior?
    - Hierarchical/multilevel modeling
Clinician

- What clinician-related variables influence adherence? Can this be quantified?
- Identifying singular variables
- Hierarchical:
  - Several patients treated by same clinician
  - Assumption of independence
  => hierarchical modeling approach
  => attribution of variance in adherence to clinician vs. outcome
Tolerance for non-adherence

- Clinician vs. patient expectations
- Clinician to patient:
  - “You should be adherent or you’ll get into trouble”
- Patient to clinician:
  - “How nonadherent can I be before I get into trouble?”
- Count versus probability

![Graph showing Complete Cytogenetic Response at Follow-up](chart.png)

| Ratio of Medication Taken to Medication Prescribed over 30 Days (pill count adherence) |
|---------------------------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|                                 | 2.1 | 1.9 | 1.8 | 1.7 | 1.6 | 1.5 | 1.4 | 1.3 | 1.2 | 1.1 | 1.0 | 0.9 | 0.8 | 0.7 | 0.6 | 0.5 | 0.4 | 0.3 | 0.2 | 0.1 | 0.0 |
Risk

• Risk:
  • Identification of risk factors
  • Deterministic models of risk assessment and consequences

• Gradient: risk-based differentiation
• Heuristic models
  • “Clusters”, “clouds”, …
  • Profiling rather typing
Adherence in clinical studies

- Endpoint or midpoint?

- Endpoint:
  - What is the adherence?
    - Is the patient adherent?

- Midpoint:
  - What is the (non-)adherence and how did it affect clinical outcomes?
    - Is the patient adherent and is the blood pressure under control?

- “Perfectly adherent to an imperfect medication regimen”
Adherence ~ clinical outcomes

• Moderator variable
  • Variable that affects the direction and/or strength of the relation between a predictor and an outcome variable.”
Adherence ~ clinical outcomes

- Mediator variable
  - Variable that accounts for the relation between the independent variable and the outcome variable

Baron & Kenny, J Pers Soc Psychol, 1984
Assessment

• Write-off (presumably) biased assessments:
  • Patient self-reports
  • Clinician assessment

• What do we need to measure for the purpose at hand?
  • Comprehensive assessment (“for the record”)
  • Clinical impression (“in practice”)
    • @ point-of-care
    • Integrated into process of care

• Facilitating assessment to overcome therapeutic inertia to deal with non-adherence
Interventions

• Adherence-enhancing interventions are becoming increasingly complex
  • Framework
  • Intervention
  • Staffing mix

• Into the future:
  • How complex can we get?

• Back to the future:
  • Should we de-complicate?

• Accessibility of interventions

Replicability

Scalability

Affordability

Sustainability
Interventions

- From “about the patient” to “patient-centric”
- Ability to integrate disease and treatment into daily life
- Functional, health, quality of life, and other priorities patients they want to preserve
- Compromises willing to make
- Psychological, social, and physical impact of adapting to disease and treatment
- Engage social network

Abraham & MacDonald, Br J Cancer 2012
Openness to challenges

Believe me, that H. pylori drink was awful!

Barry Marshall accepting the 2005 Nobel Prize for Medicine

Referees may not be open to your (gentle) argumentation