

**Developing a Program of Research:
Building Knowledge
on Patient Adherence**

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Objectives

1. Identify the developmental phases of a research career
2. Identify the funding resources and access them
3. Evaluate personal level of development and next steps

Through the views of a program of research on adherence


Why Pursue a Research Program?

Nursing has a history of caring for others with knowledge of what and how to do that passed down by more seasoned nurses

Today, health care exists in a world of science.

WE NEED EVIDENCE TO DRIVE AND SUPPORT OUR PRACTICE

Evidence Based Practice Will Improve Patient Care And Patient Outcomes



Research Will Build The Evidence To Support Effective Patient Care

**Research Contributes to the
Broader Areas of Science**

**Research Makes a Difference in the
Professional Image of Nursing**



Research Project vs. Research Program

- ◆ **Research Project – Single Study**
 - **May be part of a research program**
 - **May be a stand alone study**

Research Project vs. Research Program

- ◆ **Research Program – Series of Studies**
 - **Thematic**
 - **Pursue depth/increasing understanding**
 - **Inter-related**

Examples From My Own Program

- ◆ **Can Poor Adherence be Improved in Clinical Trial Subjects?**
- ◆ **Can Poor Adherence be Improved in a Clinical Population?**
- ◆ **Can Poor Adherence be Prevented?**
- ◆ **Is Adherence Intervention Better Delivered by Phone or Mail?**
- ◆ **Can Poor Adherence be Improved in Co-Morbid Conditions?**

What Does it Take?

- ◆ **Curiosity**
- ◆ **Passion**
- ◆ **Persistence**
- ◆ **Resilience**
- ◆ **Benefit from criticism**
- ◆ **Patience**



Developmental Phases

- ◆ Inquisitive
- ◆ Exposure
- ◆ Preparation
- ◆ Apprenticeship
- ◆ Mentored Research
- ◆ Independent Research
- ◆ Collaborative 'Big Science' Research
- ◆ Research Mentor/Facilitator

Be Sure the Necessary Skills are Present

- ◆ Writing Skills
- ◆ Methodological Expertise ... in the Area
- ◆ Ability to Accept Criticism
- ◆ Flexibility in Planning
- ◆ Ability to Work in and to Lead a Team
- ◆ Ability to Persist in the Face of Frustration
- ◆ Willingness to Revise and Redo

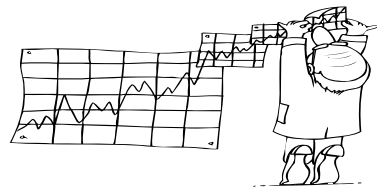
Examples

- ◆ Undergraduate Research Experience
- ◆ Graduate Education
 - Research Assistant
 - Research Projects - Mentored
- ◆ Research Staff - Mentored
- ◆ Independent NIH Funded Research
- ◆ Center Grant
- ◆ Student/Faculty Mentor, Consultant

Building a Research Program
Takes Time



What are the Key Steps in Developing
One Specific Research Trajectory?



Importance of the Science

- ◆ Who Cares? / So What?
- ◆ Will It Have Impact?
- ◆ Does It Impact a Significant Number of Persons?
- ◆ Will It Save Costs?



Importance: Examples from Patient Adherence

1. Approximately 40-60% of Patients will Fail to Follow Treatment Recommendations
2. Disease Outcomes are Poorer than Expected
3. Disease Progression and Complications Cost Over \$100 Billion
4. Few Studies Point to How to Improve Adherence Rates

What is the Next Step Needed In the Science?

- ◆ What Has Already Been Learned?
[don't be redundant]
- ◆ What Do We Need to Know Before Moving Forward?



Take the Next Question to Be Answered Be Innovative Be Methodically Sound



Next Steps: Examples from Patient Adherence: 5 Studies

1. An Intervention Study to Improve Poor Adherence in a Clinical Trial (Prevention, Asymptomatic)
2. An Intervention Study to Improve Poor Adherence in Clinical Practice Sites (Treatment, Symptomatic)
3. Adherence in Clinical Trials – An Induction Study (Prevention, Asymptomatic)
4. An Intervention Study to Improve Poor Adherence by Phone or Mail (Treatment, Symptomatic)
5. An Intervention Study to Improve Poor Adherence in Co-Morbid Conditions (Treatment, Asymptomatic & Symptomatic)

All Used RCT Design and Were Built
on Findings from Previous Studies

**What Did We Learn
and
How Did We Build?**



**Study 1: Clinical Trial, Hyperlipidemia
N=60**

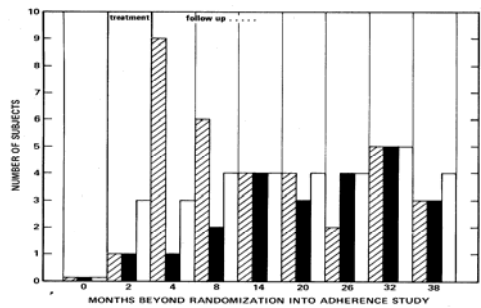
1. Adherence could be improved in clinical trial sample
2. But, declined without sustained intervention
3. Adherence distribution was J-shaped
4. Adherence patterns varied across persons
5. Greater variability led to overestimates of adherence
6. Initial behavior predicts long-term behavior

**Proportion of Subjects
≥ 75% Compliance**

	Pre-intervention	Post-Intervention*
Experimental	0	9
Attention Control	0	1
Usual Care	0	3

* $\chi^2 = 10.21, 2df, p = .006$

Maintenance of Compliance



**Variability in Adherence and
Treatment Response**

- ◆ Greater response to monitoring/attention
 - overestimated compliance (r = .75)
 - greater variability (r = .50)
- ◆ Relationship between variability and overestimation (r = .54)

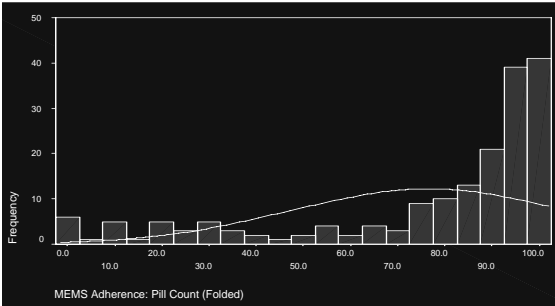
Behavior as a Predictor of Adherence

Initial Adherence at 1 Month as Predictor of Adherence at Year 1 = $R^2 = .345$ $p \leq .0001$

(Dunbar & Knoke, 1986)

Variable	Year 1 Adherence		Year 7 Adherence	
	Coeff (P)	r ² (P)	Coeff (P)	r ² (P)
Intercept	6.77		8.1	
Age	0.24 (.01)		0.4(<.001)	
Cig/Day	-0.17 (<.001)		-0.03 (<.001)	
Psych Distress	-0.83 (<.01)		-1.7 (<.001)	
1 Month Adh.	0.71 (<.001)	.36 (<.001)	0.6 (<.001)	.24 (<.001)

Electronically Monitored Adherence (Pill Count)



Study 2: Clinical Sample, Rheumatoid Arthritis N=135

1. Adherence can be improved in clinical sample
2. Electronic measures predicted clinical outcome (pain)
3. Session attendance associated with adherence change
4. Adherence patterns vary across persons
5. Frequency of dosing associated with adherence level
6. Electronic measures more likely to detect poor adherence
7. Predictors of adherence vary by measurement method

Results

Group Differences Baseline To End Of Treatment

◆ <u>Average Change In Adherence</u>	\bar{x}	sd
Intervention	4.30	± 24.7
Usual Care	-7.99	± 27.1
	$t = -2.02,$	$p = .023$
◆ <u>Proportion Greater Than 80% Adherence</u>		
Intervention + Maintenance	=	29.7%
Usual Care	=	15.6%
	$\chi^2 = 2.25,$	$df = 1, p = .065$

Relationship of Change in Adherence and Functional Status

	Tx	F/U
Δ Adherence: Δ Pain	$r_s = .02$ (n = 96)	$r_s = -.22^*$ (n = 98)
Δ Adherence: Δ Difficulty	$r_s = .04$ (n = 95)	$r_s = -.11$ (n = 97)
Δ Adherence: Δ Assistance	$r_s = .03$ (n = 96)	$r_s = -.12$ (n = 97)

* $p < .01$ Changes in adherence were associated with changes in pain in carrying out activities of daily living, but no level of difficulty or assistance required

Predictors of Change

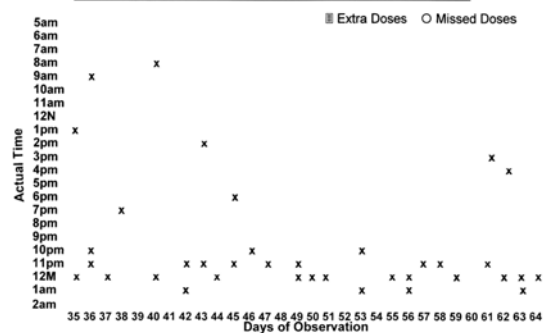
Baseline Correlates With Change Score

End of Treatment $r_s = -.20$ $p = .036$
Follow-up $r_s = -.32$ $p = .001$

Session Attendance and Change Score

Follow-up $f = 9.07, df = 2, p = .0007$

Twice a Day Dosing Prescription



Reported Adherence: Self-Reported vs. MEMs Cap

Adherence in Rheumatoid Arthritis

	Eligible	Ineligible
Self-Report	24 (6.7%)	336 (93.3%)
MEMs Cap	140 (53.4%)	122 (46.6%)

Detection of Poor Adherence: Diary vs. EEM

Number of Ss Taking $\geq 80\%$, $< 80\%$ of Doses (N = 58)

	$\geq 80\%$	$< 80\%$
Diary total	29	29 (50.0%)
EEM total	27	31 (53.4%)

$\chi^2 = 3.395$, $df = 1$, $p = .113$

Kappa = .241

Diary - EEM Match	17	19
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RAC-1

Predictors of Adherence by Measurement Method

	Monitored	Interview	24-hr. Recall
Gender	X		
Employment	X		
Income	X		
Tangible Support	X		
Symptom Support	X		
Symptom Severity	X		
Age		X	
Cost of Medication		X	
Ethnic Group			X

Dunbar-Jacob J, Sereika S, Rohay JM, Burke LE, & Kwok CK. Predictors of Adherence: Event monitoring vs. self-report.

Study 4: Clinical Sample, Rheumatoid Arthritis N=233

1. Poor sleep is related to poor adherence
2. Overall declines in adherence over time
3. No difference in good/poor adherer trajectory over time

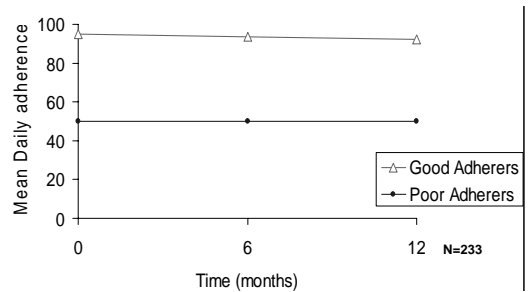
Results of Trials

◆ 18/36 Improved Medication Adherence

◆ 16/36 Improved Treatment Outcomes

Haynes, R.B., McDonald, H., Garg, A.X., Montague, P. (2002). Interventions for helping patients to follow prescriptions for medications. [Systematic Review] *Cochrane Consumers & Communication Group* *Cochrane Database of Systematic Reviews*.

Daily Adherence-Good vs. Poor Adherers



**Study 5: Clinical Sample, Co-morbid Conditions
N=267**

1. Adherence varies by medication
2. Adherence is related to number of co-morbidities
3. Adherence is not related to number of medications
4. Depression is not related to monitored adherence, but is to self-reported adherence

Days Adherent (EEM) at baseline

	<u>M</u>	sd	range
Hypertension Medication	88.1	17.4	0-100
Cholesterol Medication	82.7	19.6	9-100
Diabetes Medication	81.7	22.8	0-100

CMS 2008

Relationship of Co-Morbidities to Days Adherent

Diabetes: $r_s = -.132, p \cong .034$

No. of Co-Morbidities	Days Adherent		Total
	<80%	≥80%	
<4	12 (23%)	40 (77%)	52
5-7	37 (31.6%)	80 (68%)	117
>8	34 (38.6%)	54 (61%)	<u>88</u>
			257

Hypertension: $r_s = -.148, p \cong .017$

No. of Co-Morbidities	Days Adherent		Total
	<80%	≥80%	
<4	4 (7.7%)	48 (92.3%)	52
5-7	19 (16.4%)	97 (83.6%)	116
>8	19 (21.8%)	69 (79%)	<u>87</u>
			255

Self-report: $r = .091, p = .15$

CMS 2008

Is Depression (Beck 2) Related to Adherence?

Adherence Measure	R ²	df	F	p ^a
Diabetes EEM	.012	1,255	3.01	.084
Hypertension EEM	.000	1,255	0.113	.737
Self-Report	.040	1,250	10.404	.001

^a p two-sided

CMS 2008

What Have We Learned Overall

1. Adherence can be improved with intensive intervention, but maintenance is a challenge
2. Adherence patterns vary across persons, but the temporal trajectory is downward
3. Measures differ in the information given, but electronic monitoring best predicts clinical change
4. Behavioral and environmental traits are important, including initial behavior, regularity, sleep
5. Co-morbidities pose particular challenges

Where Do We Go Next?

1. Target Initial Period of Medication Taking
2. Identify Clusters of Adherence Patterns and Examine Correlates
3. Examine Regimen/Education Challenges in Co-Morbidities
4. Other

The Role of Preliminary Studies



Assess Feasibility

- ◆ Can You Recruit and Retain Subjects?
- ◆ Can You Collect the Necessary Information?
- ◆ Can You Deliver the Intervention Reliably?
- ◆ Is the Intervention Likely to Work?
- ◆ Are There Unexpected Issues to be Addressed?

What Resources Are Necessary to Move Forward?



Resources

- ◆ Participants
- ◆ Teammates (interdisciplinary)
- ◆ Money



Build the Research Team

- ◆ What Expertise Is Needed?
- ◆ Who Would Be Interested?
- ◆ Develop Joint Publications

Where Do You Find Help?

- ◆ Students: Research Practica & Independent Studies
- ◆ Fellow Faculty With Similar Interests
- ◆ Clinical Colleagues Interested in a Research Experience
- ◆ Student Consultation Seminars
- ◆ Auditing of Courses
- ◆ Professional Association, Consultants or Mentors



TIME



**“You will never find time for anything.
If you want time, you must make it.”
-Charles Buxton**

FUNDING SOURCES



Money is Something You Search For

- ◆ Many Small Pots of Money Exist
- ◆ Apply to As Many As Possible
- ◆ Buy Help, Supplies/Equipment
And Your Time If Possible
- ◆ Join Colleagues Who
Have Resources



Training Monies: Student

- ◆ Individual Fellowships
 - NIH
 - Professional Organizations
- ◆ Institutional Training Grants
- ◆ Graduate Assistantships

Training Monies: Faculty

- ◆ Post-Doctoral Fellowships
 - NIH
 - Professional Organizations
 - Institutions
- ◆ Mentored Research Grants
 - NIH
 - Institutional
- ◆ Collaboration/Junior Investigator

Develop Funding Strategies

- | | |
|-------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|
| A. Small Studies <ul style="list-style-type: none">■ Internal■ Foundation■ State | C. Larger Scale
(R01 & Equivalent Studies) <ul style="list-style-type: none">■ Foundation■ NIH |
| B. Moderate Studies <ul style="list-style-type: none">■ Foundation■ State■ NIH | |

Criteria For Success

- ◆ Significant
- ◆ Innovative
- ◆ Methodologically Sound
- ◆ Environment



Where Do You Go Next?

- ◆ Move on to Increasingly Independent Sources of Funding
- ◆ Build Depth in Science Area
- ◆ Publish
- ◆ Begin to Mentor Others
- ◆ Continue to Collaborate



Move Forward From Where You Are

GREAT MOMENTS IN SCIENCE

