HYPERTENSION ADHERENCE & PERSISTENCE

Maribel Salas MD, DSc, FACP, FISPE 4th Training Workshop and Symposium at MURIA University of Namibia, Windhoek, ISPE & ISPE African Chapter 18 – 21 June 2018

Some Key Concepts....

Compliance

- From Latin "complire" to fill up, to complete an action, transaction or process
- 'The acting in accordance with, or the yielding to a desire, request, condition, direction, etc.; a consenting to act in conformity with; an acceding to; practical assent.' (Oxford English Dictionary)
- <u>Acting in accordance with advice</u>, in this case advice given by the prescriber. It implies "a <u>paternalistic attitude</u> towards the patient on the prescriber's part and that it should not be used'.

Br J Clin Pharmacol. 2007 Apr; 63(4): 383-384.

Adherence

 From the Latin word adhaerere, which means to cling to, keep close, or remain constant. It implies the tenacity that patients need to achieve in sticking to a therapeutic regimen.

Br I Clin Pharm



- Adherence. Definitions "The extent to which the patient follows medical
- instructions" (WHO, 2001)
- "The extent to which a person's behavior <u>coincides</u> with medical or health advice" (Haynes)
- "The extent to which a <u>patient acts in accordance</u> with the prescribed interval and dose of a dosing regimen (<u>timing</u>, <u>dosage</u> and <u>frequency</u>) (ISPOR)"
- Comprises initiation, implementation, and discontinuation
- "The extent to which a person's behaviour taking medication, following a diet, and/or executing lifestyle changes, <u>corresponds with agreed recommendations</u> from a health care provider" (Haynes & Rand)

Value in Health, 2013; 16: 863-871

Compliance or Adherence?

col. 2007 Apr: 63(4): 383-384.

- Adherence requires the **patient's agreement** to the recommendations
- Compliance implies patient is only following indications

However,

· Many researchers use those terms interchangeably

World Health Organization, 2001

Persistence. Definition

. The time of continuous therapy:

- · Time from initiation of therapy to discontinuation of therapy
- The length of time between initiation and the last dose immediately preceding discontinuation



Adherence/Compliance vs. Persistence

- Two different constructs
- Medication adherence (compliance) refers to the degree or extent of conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage, and frequency.
- Medication persistence refers to the act of continuing the treatment for the prescribed duration. It may be defined as "<u>the duration of time from initiation to</u> discontinuation of therapy."

Value Health. 2008 Jan-Feb;11(1):44-7.







Persistence with Treatment for Hypertension in Actual Practice. Caro JJ, Salas M, Speckman JL, Raggio G, Jackson JD.

- Cohort study of patients with diagnosis of hypertension, treated between 1989 and 1994 and included in the Saskatchewan Health databases. Patients with concurrent diagnoses likely to affect initial treatment choice were excluded.
- There were 79,591 subjects grouped into those with established hypertension (52,227 [66%]) and those with newly diagnosed hypertension (27,364 [34%]).
- Persistence with antihypertensive therapy decreased in the first 6 months after treatment was started and continued to decline over the next 4 years. Of the patients with newly diagnosed hypertension, only 78% persisted with therapy at the end of 1 year, as compared with 97% of the patients with established hypertension (p < 0.001).
- Barriers to persistence occur early in the therapeutic course and that achieving successful therapy when treatment is started is important to maintaining long-term persistence.

CMAJ. 1999 Jan 12;160(1):31-7.





Odds Ratio of Persistence with Antihypertensive Drug Therapy through the 1st year for patients in Saskatchewan, 1989-1994

Characteristic	A	patients = 74 181	Patients with newly diagnosed hypertensio n = 22 875	
Established hypertension	10.73	(10.01-11.49)	-	
Female sex	1.16	(1.10-1.23)	1.10 (1.03-1.18)	
Age ≥ 60 yr	1.11	(1.05-1.18)	1.08 (1.01-1.16)	
Hospital admission	0.75	(0.70-0.81)	0.80 (0.74-0.87)	
> 5 physician visits in previous yr	1.59	(1.48-1.71)	1.93 (1.78-2.11)	
> 3 other prescriptions in previous year	1.29	(1.22–1.37)	1.30 (1.21–1.39)	
			CMAJ, 1999; 160(1)	



Effect of initial drug choice on persistence with antihypertensive therapy: the importance of actual

practice data. Caro JJ, Speckman JL, Salas M, Raggio G, Jackson JD

- Using the Saskatchewan database, all outpatient prescriptions for antihypertensive medications filled between 1989 and 1994 were analyzed.
- 22,000 patients with newly diagnosed hypertension whose initial treatment was with a diuretic, beta-blocker, calciumchannel blocker or angiotensin-converting-enzyme (ACE) inhibitor were included. Rates of persistence over the first year of treatment were compared.
- After 6 months, persistence with therapy was poor and differed according to the class of initial therapeutic agent: 80% for diuretics, 85% for beta-blockers, 86% for calcium-channel blockers and 89% for ACE inhibitors (p < 0.001). Changes in the therapeutic regimen were also associated with lack of persistence.

CMAJ. 1999 Jan 12;160(1):41-6.

HYPERTENSION: ADHERENCE & PERSISTENCE

Medication Adherence in Hypertension

- Poor medication adherence is the main cause of failure to control hypertension
- A quarter of patients who are newly initiated on antihypertensive therapy fail to fill their first prescription
- During the first year of treatment, the average patient is on antihypertensive medications for only 50% of the time
- One patient in five has sufficiently high adherence during the first year of treatment to achieve the benefits observed in clinical trials







Trust, Medication Adherence, and Hypertension Control in Southern African American Men

Elder K, Ramamonjiarivelo Z, Wiltshire J, et al

- The relationship between trust in the medical system, medication adherence, and hypertension control in Southern African American men was studied.
- The sample included <u>235 African American men aged 18</u> years and older with hypertension.
- African American men with higher general trust in the medical system were more likely to report better medication adherence (odds ratio [OR] = 1.06), and those with higher self-efficacy were more likely to report better medication adherence and hypertension control (OR = 1.08 and OR = 1.06, respectively).

Characteristic	Total, % (No.)	Trust, Medication Adhe	rence, and
Age, y		Hypertension Control in	n Southern Afric
≤ 34	3.4 (8)	American Men, Birming	ham, AL, 2007–20
35-44	11.1 (26)	(N=235)	
45-54	39.6 (93)	1	
55-64	37.0 (87)	Income, \$	
≥ 65	8.9 (21)	< 5000	32.9 (72)
Married		5000-11 999	31.1 (68)
Yes	32.3 (76)	12 000-15 999	13.2 (29)
No	67.7 (159)	> 16 000	10.E (E0)
Insurance type		210000	22.0 (30)
Public	88.1 (207)	Usual source of care	
No insurance	11.5 (27)	Yes	99.6 (234)
Private	0.4 (1)	No	0.4 (1)
Perceived health status		Medication adherence	
Very good/excellent	9.4 (22)		57.0 (JOD)
Good	30.2 (71)	Yes	57.3 (134)
Fair	53.6 (126)	No	42.7 (100)
Poor	6.8 (16)	Hypertension controlled	
Education		Yes	21 (49)
< high school	21.7 (51)	N-	21 (40)
High school	15.3 (36)	NO	79 (184)
Some college	52.3 (123)		
College degree	10.6 (25)	Am J Public Hea	alth. 2012. Dec:102(12):2242-5.

Selected Results from Logistic Regressions Models of Medication Adherence and Hypertension Control: Trust, Medication Adherence, and Hypertension Control in Southern African American Men, Birmingham, AL, 2007–2010

	Medication Adher	ence	Hypertension Con	trol
Characteristics	OR (95% CI)	Р	OR (95% CI)	Р
General trust	1.06 (1.00, 1.11)	.027	0.954 (0.902, 1.01)	.105
Perceived discrimination	0.666 (0.317, 1.40)	.287	0.99 (0.416, 2.37)	.989
Perceive racism	0.987 (0.934, 1.04)	.668	1.02 (0.956, 1.09)	.567
Self-efficacy	1.08 (1.02, 1.13)	.002	1.06 (1.00, 1.12)	.048
Participate in medical decision-making	0.974 (0.866, 1.09)	.655	1.01 (0.881, 1.15)	.899
Medication adherence			0.903 (0.424, 1.92)	.792

Note. CI = confidence interval; OR = odds ratio. Models also adjusted for age, marital status, education, income, and perceived health status. Answering "yes" to any of the 4 questions of the Morisky scale indicates worse adherence. Hypertension control is defined as blood pressure \leq 140/90.



Reported Racial Discrimination, Trust in Physicians, and Medication Adherence among Inner-city African

Americans with Hypertension. Cuffee YL, Hargraves JL, Rosal M, et al

- To determine if reported racial discrimination was associated with medication nonadherence among African Americans with hypertension and if distrust of physicians was a contributing factor.
- Was a contributing tactor. Data were obtained from the TRUST project conducted in Birmingham, Alabama, 2006 to 2008. <u>African Americans diagnosed with hypertension and receiving care</u> at an inner city, safety net setting were included. Three categories of increasing adherence were defined based on the Morisky Medication Adherence Scale. Trust in physicians was measured with the Hall General Trust Scale, and discrimination was measured with the Experiences of Distribution Parts. Discrimination Scale.
- There were 227 African American men and 553 African American women, with a mean age $\begin{array}{l} \text{ for $15,7\pm9$ were 42 minimum instrume and $15,7\pm9$ were 15 confidence interval = 17%, 100%) of the association between discrimination and medication adherence.
- Racial discrimination was associated with lower medication adherence, and this association was partially mediated by trust in physicians. Patient, physician and system approaches to increase "earned" trust may enhance existing interventions for promoting medication adherence.

Am J Public Health. 2013 Nov;103(11):e55-62

TABLE 1—Characteristics of African American Participants With Hypertension by Adherence Level: TRUST Study, Birmingham, AL, 2007-2008

		Adherence Levels"			
Variable	Low (n = 112)	Moderate (n = 350)	High (n = 318)	P	
Discrimination, mean ^b	4.05	3.58	2.88	.025	
Age, mean	50.79	53.58	54.83	< .001	
Gender, %				.018	
Male	8.81	48.02	43.17		
Female	16.64	43.58	39.78		
Education, %				.315	
< high school	14.07	46.67	39.26		
High school	21.05	42.11	36.84		
Some college	13.82	44.74	41.45		
College degree	8.00	46.67	45.33		
Annual household income, %				.281	
< \$5000	16.89	48.86	34.25		
\$5,0000-\$11 999	14.67	43.63	41.70		
\$12 000-\$15 999	11.20	41.60	47.20		
≥\$16 000	11.57	47.93	40.50		
Trust, mean ^o	36.53	38.53	40.84	<.001	

TABLE 2–Ordinal Logistic Regression Model for the Association Between Reported Discrimination and Medication Adherence Among African American Participants: TRUST Study, Birmingham, AL, 2007-2008

	Model 1		Model 2		
Variable	Cumulative OR (95% CI)	В	Cumulative OR (95% CI)	i) B	
Discrimination [®]	0.94 (0.91, 0.97)	-0.145	0.96 (0.93, 1.00)	-0.089	
Trust ^b			1.04 (1.02, 1.06)	0.175	
Age	1.02 (1.01, 1.04)	0.118	1.02 (1.01, 1.03)	0.104	
Gender (Ref: male)	0.64 (0.47, 0.87)	-0.109	0.72 (0.52, 0.98)	-0.080	
Education (Ref: < high school)					
High school	0.79 (0.48, 1.31)	-0.043	0.74 (0.45, 1.23)	-0.056	
Some college	1.26 (0.85, 1.85)	0.060	1.26 (0.86, 1.87)	0.061	
College degree	1.86 (1.04, 3.34)	0.099	2.01 (1.12, 3.63)	0.110	
Annual household income, \$ (Ref: < 5000)					
5000-11 999	1.31 (0.93, 1.85)	0.070	1.31 (0.92, 1.85)	0.067	
12 000-15 999	1.62 (1.05, 2.48)	0.097	1.61 (1.05, 2.48)	0.095	
≥ 16 000	1.23 (0.80, 1.90)	0.042	1.20 (0.78, 1.85)	0.036	

Note C = confidence intervel; OR = odds ratis. The sample size was 724. These category medication adherence was derived by self-report from the Morking scale. "The Kinger Expension State Intervence State Intervence State State Intervence State

tiveh

Am J Public Health. 2013 Nov;103(11):e55-62



INTERVENTIONS OF COMPLIANCE (ADHERENCE). HYPERTENSION AS AN EXAMPLE ISPOR GROUP: DETERMINANTS OF COMPLIANCE & PERSISTENCE WORKING GROUP

Maribel Salas (Chair), Femida Gwadry-Sridhar, Lincy Lal, Anuja Roy, Elizabeth Manias, Joanne LaFleur, Veronica Decker, Sangeeta Budhia, John Zeber, Dyfrig Hughes, Judy Shinogle, Jasmanda Wu, Monali Bhosle Andrew M. Peterson, Peter Dale Systematic Review of Interventions to Improve Compliance

Impact of interventions on medication adherence and blood pressure control in patients with essential hypertension: a systematic review by the ISPOR medication adherence and persistence special interest group. Gwady-Sidhar FH, Manias E, Salas M, Hughes DA, Ratzki-Leewing A, Grubisic M. OBJECTIVES: To systematically review the evidence on the impact of interventions to improve medication adherence in adults prescribed antihypertensive medications. METHODS: An electronic search was undertaken of articles published between 1979 and 2009, without language restriction, that focused on interventions to improve antihypertensive medication adherence among patients (218 years) with essential hypertension. Studies must have measured adherence as an outcome of the intervention. We followed standard guidelines for the conduct and reporting of the review and conducted a narrative synthesis of reported data.

RESULTS: <u>Ninety-seven articles</u> were identified for inclusion; 35 (35 of 97, 36.1%) examined interventions to directly improve medication adherence, and the <u>majority (58 of 97, 59.8%)</u> were randomized controlled trials. Thirty-four (34 of 97, <u>35.1%) studies reported a statistically</u> significant improvement in medication adherence.

DISCUSSION/CONCLUSIONS: Interventions aimed at improving patients' knowledge of medications possess the greatest potential clinical value in improving adherence with antihypertensive therapy. However, we identified several limitations of these studies, and advise future researchers to focus on using validated adherence measures, well-designed randomized controlled trials with relevant adherence and clinical outcomes, and guidelines on the appropriate design and analysis of adherence research.



RCT in Compliance: Heterogeneity of Metanalysis

- Population
- Diagnosis
- Type of Intervention
- Compliance definition & measures

Value in Health, 2013; 16: 863-87

- Outcomes (number, type & measures)
- Statistical analysis

Main Methodological Findings

- Interventions were not guided by conceptual model of the determinants of non adherence
- Interventions were not validated
- Interventions provided limited information on different adherence components (initiation, implementation and discontinuation)
- There is limit description of interventions
- The quantification and measurement of medication adherence were inconsistent (e.g. qualitative measure –adherence yes/no; quantitative – continuous measure)

Value in Health, 2013; 16: 863-871

Continuation....

- · Components of medication adherence were inadequately described
- Studies did not measure BP or other clinical biomarker
- · Scales to measure adherence were inconsistent across studies (self-reporting to electronic monitoring devices)
- · Adherence rates and blood pressure were poorly reported.
- Limited information reported on dropouts and loss to follow-up

Value in Health, 2013; 16: 863-871

Conclusions from RCT...

- No single intervention to improve patient compliance is consistently effective
- Adherence/Compliance is a <u>multi-factorial issue</u>
- Interventions should target multiple components: educational, structural, and organization of the health care system.
- The most effective interventions are those focused on: improving clinical interactions, involving patients in healthcare decisions, promoting patient education and self-management, and improvements at the system level
- More quantitative information reported in RCT will allow more robust analysis.

Contributions to Literature

Key Message

Educational strategies provide benefits in reducing non-adherence

The most effective interventions to improve compliance with lipid lowering medications are complex, multi-factorial interventions.

Smartphone apps for improving medication adherence in hypertension: patients'

perspectives. Morrissey EC, Casey M, Glynn LG, Walsh JC, Molloy GJ

- Digital interventions, such as <u>smartphone applications (apps</u>), are becoming an increasingly common way to support medication adherence and self-management in chronic conditions.
- The aim of this study was to explore patients' perspectives on smartphone apps to improve medication adherence in hypertension.
- Qualitative study based in the West of Ireland. <u>Twenty-four patients with</u> hypertension were purposively sampled and engaged in focus groups. Thematic analysis on the data was carried out.
- Largens on use data was carried out. Participants ranged in age from <u>50 to 83 years</u> (M=65 years) with an equal split between men and women. Three major themes were identified in relation to patients' perspectives on smartphone apps to improve medication adherence in hypertension: "development of digital competence," "rules of engagement," and "sustainability" of these technologies.
- Sustainability of these technologies. These data showed that patients can identify the **benefits of a medication reminder and recognize that self-monitoring their blood pressure** could be empowering in terms of their understanding of the condition and interactions with their general practitioners. There are concerns about increasing health-related anxiety and doubts about the sustainability of this technology over time.

Patient Prefer Adherence, 2018 May 14:12:813-822

AIDES Method

- · Derived from a metanalysis of 153 studies of interventions to improve adherence, where combined cognitive behavioral and affective interventions were more effective than single interventions
- · Method for improving adherence to medications:

	Action	Activity
Α	Assessment	Assess all Medications
I	Individualization	Individualize the regimen for a patient
D	Documentation	Provide written documentation
E	Education	Provide accurate and continuing education tailored to the needs of the individual
S	Supervision	Provide continuing supervision of the regimen

Culturally Appropriate Storytelling to Improve Blood Pressure: a Randomized Trial. Houston TK, Allison JJ, Sussman M, Hom W, Holt CL, Trobaugh J, Salas M, Pisu M, Cuffee YL, Larkin D, Person SD, Barton B, Kiefe CI, Hullett S. Storytelling is emerging as a powerful tool for health promotion in vulnerable populations. However, these interventions remain largely untested in rigorous studies. To test an interactive <u>storytelling intervention involving DVDs</u>. Randomized, controlled trial in which comparison patients received an attention control DVD. Separate

- random assignments were performed for patients with controlled or uncontrolled hypertension (ClinicalTrials.gov registration number: NCT00875225) African Americans with hypertension from an inner-city safety-net clinic in the southern United States were included. 3 DVDs that contained patient stories. Storytellers were drawn from the patient population.
- Outcomes were differential change in blood pressure for patients in the intervention vs. the comparison group at baseline, 3 months, and 6 to 9 months.
- group at baseline, 3 months, and 6 to 9 months. 299 African American patients were randomly assigned between December 2007 and May 2008, 76.9% were retained throughout the study, 71.4% were women, and the mean age was 53.7 years. Baseline mean systolic and diastice pressures were similar in both groups. Among patients with baseline uncontrolled hypertension, reduction favored the intervention group at 3 months for both systolic (11.21 mm Hg) [5% Cl.2.51 to 19.9 mm Hg]; P = 0.012) and diastolic (6.43 mm Hg [Cl, 1.49 to 11.45 mm Hg]; P = 0.012) blood pressures.
- The storytelling intervention produced substantial and significant improvements in blood pressure for patients with baseline uncontrolled hypertension. Funding: Finding Answers: Disparities Research for Change, Robert Wood Johnson Foundation.

Ann Intern Med. 2011 Jan 18:154(2):77-



ne stics
tics
tics
onto
2 12 ATE 1
ento
in
γP
ont
ent





Subgroup and Measure	Baseline	3 Months	6-9 Months	
All patients				
Patients, n	299	231	231	
Systolic blood pressure, mm Hg				
Comparison	132.80	134.12	138.42	M O C F
Intervention	133.18	128.03	132.38	Ivlean Systolic and
Diastolic blood pressure, mm Hg				
Comparison	76.19	78.56	81.27	Diastolic Blood
Intervention	76.89	76.21	79.30	Diastolic Dioou
Controlled hypertension at baseline				Pressures, by
Patients, n	172	136	138	
Systolic blood pressure, mm Hg				Subaroup
Comparison	120.37	125.56	130.43	Oubgroup,
Intervention	117.63	121.70	127.21	Accortainment
Diastolic blood pressure, mm Hg				Ascentainment
Comparison	70.89	75.17	78.31	
Intervention	69.05	73.52	75.59	Time, and
Uncontrolled hypertension at baseline†				Hypertension
Patients, n	123	93	89	Control Ctoture et
Systolic blood pressure, mm Hg				Control Status at
Comparison	153.06	147.16	149.84	
Intervention	152.35	135.24	137.19	Baseline*
Diastolic blood pressure, mm Hg				Babolino
Comparison	84.92	83.96	85.70	
Intervention	86.62	79.23	83.18	
Blood pressure measurements were obt y the World Health Organization. Una nal data analyses based on random-ef	ained accord idjusted mea fects models	ling to a proto ns were taken that nested	col established i from longitu- repeated blood	



	Estimated Regression Coefficient (95% CI)*	P Value	Estimated Regression Coefficient (95% CI)*	P Value
All patients				
Systolic blood pressure	6.53 (1.29 to 11.26)	0.014	6.41 (1.04 to 11.77)	0.019
Diastolic blood pressure	3.05 (-0.10 to 6.21)	0.058	2.66 (-0.60 to 5.94)	0.109
Controlled hypertension at baseline				
Systolic blood pressure	1.12 (-4.71 to 6.95)	0.71	0.44 (-5.74 to 6.63)	0.89
Diastolic blood pressure	-0.19 (-3.394 to 3.55)	0.92	0.88 (-3.10 to 4.86)	0.67
Uncontrolled hypertension at baseline				
Systolic blood pressure	11.21 (2.51 to 19.91)	0.012	11.9 (3.27 to 20.59)	0.007
Diastolic blood pressure	6.43 (1.40 to 11.45)	0.012	4.22 (-1.07 to 9.52)	0.119
			Ann Intern Me	<i>t.</i> 2011;154:77-

African American Veterans Storytelling: A Multisite Randomized Trial to Improve Hypertension. Houston TK, Fix GM, Shimada SL, et al

- Disparities in hypertension control persist for African American Veterans.
 To enhance cultural relevance of hypertension control self-management education, in a multisite, stratified randomized trial, we tested an interactive Veteran-to-Veteran storytelling digital video disk (DVD) intervention created with Veteran partners, versus an education-only DVD comparison.
- At 3 VA facilities, African American Veterans with uncontrolled hypertension were randomized to storytelling DVD intervention or didactic comparison DVD and followed for 6 months.
- African American Veterans (N=619) were 92% male, 39% over age 65, most had a high-school education, over 50% of both the intervention and comparison group propoted a household income of <\$20,000, and 40% had less than adequate health literacy.
- No differences between the intervention and control groups were statistically significant (all P>0.3). Site differences were large; at one, the intervention group improved while the comparison groups deteriorated, resulting in 6.3 and 3.9 mm Hg more improvement for the intervention group in SBP and diastolic BP (P=0.06 and 0.04), respectively; at the other 2 sites, there were positive and negative changes, all small, in the 2 measures, with minimal differences-one site favored the comparison group and the other, the intervention
- In this multisite trial, we did not find a significant overall storytelling intervention effect Med Care. 2017 Sep.55 Suppl 9:580-584

Exercise

 In groups of 2-3 participants each discuss what are the reasons of failure of the storytelling intervention in the VA study

In Conclusion....