

# Drug Adherence: Challenges and Strategies

Update in Geriatrics  
Drugs in the Elderly  
Too Many of Too Few

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# A focus on **Medication Adherence** helps get more out of medications



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# Non adherence

- Poorer health outcomes
- Higher mortality
- Increased health care costs
- More hospitalizations that could have been avoided
- An important modifiable aspect of chronic disease management

# A meta-analysis of the association between adherence to drug therapy and mortality

(Simpson SH et al BMJ 2006)

- Meta-analysis of observational studies
- 21 studies (46 847 participants)
- (n=21) Good adherence associated with lower mortality
  - (OR 0.56, 95% CI 0.50 to 0.63) vs poor adherence
- (n=8) Good adherence to placebo associated with lower mortality
  - (0.56, 95% CI 0.43 to 0.74)
- (n=2) Good adherence to harmful drug therapy associated with increased mortality
  - (2.90, 95% CI 1.04 to 8.11).

Similar results: Simpson RJ and Mendys P, Journal of Clinical Lipidology 2010

# Non Adherence associated with poorer health outcomes in osteoporosis

(Ross S et al 2011 (MA); Imaz I et al, 2010 (MA))

- Fracture risk increases by about 16-46% with nonadherence to osteoporosis medications
  - RR 1.29 [95% CI 1.22-1.38] (Ross S et al 2011)
- Lower for non-vertebral (16%) and hip (28%) than for clinical vertebral fractures (43%). (Imaz I et al, 2010)

MA= meta-analysis

# BUT sometimes non adherence is a good thing

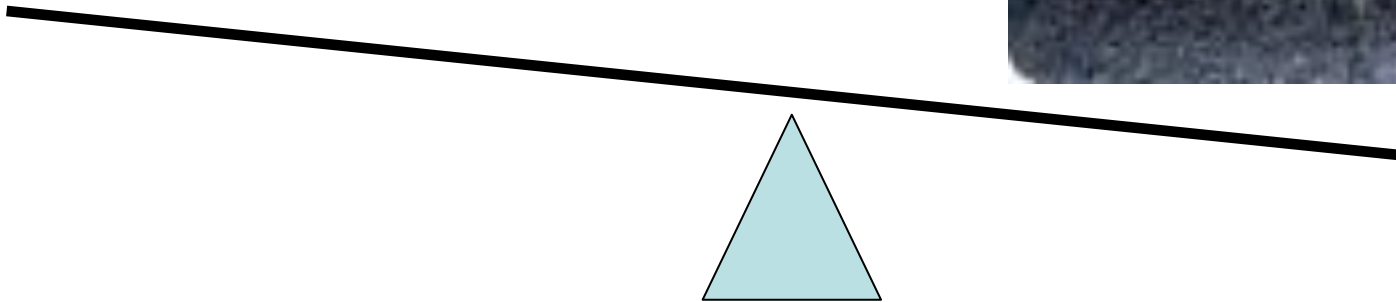
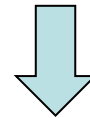
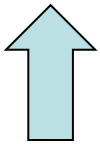


"Has the medication had any other  
side effects?"

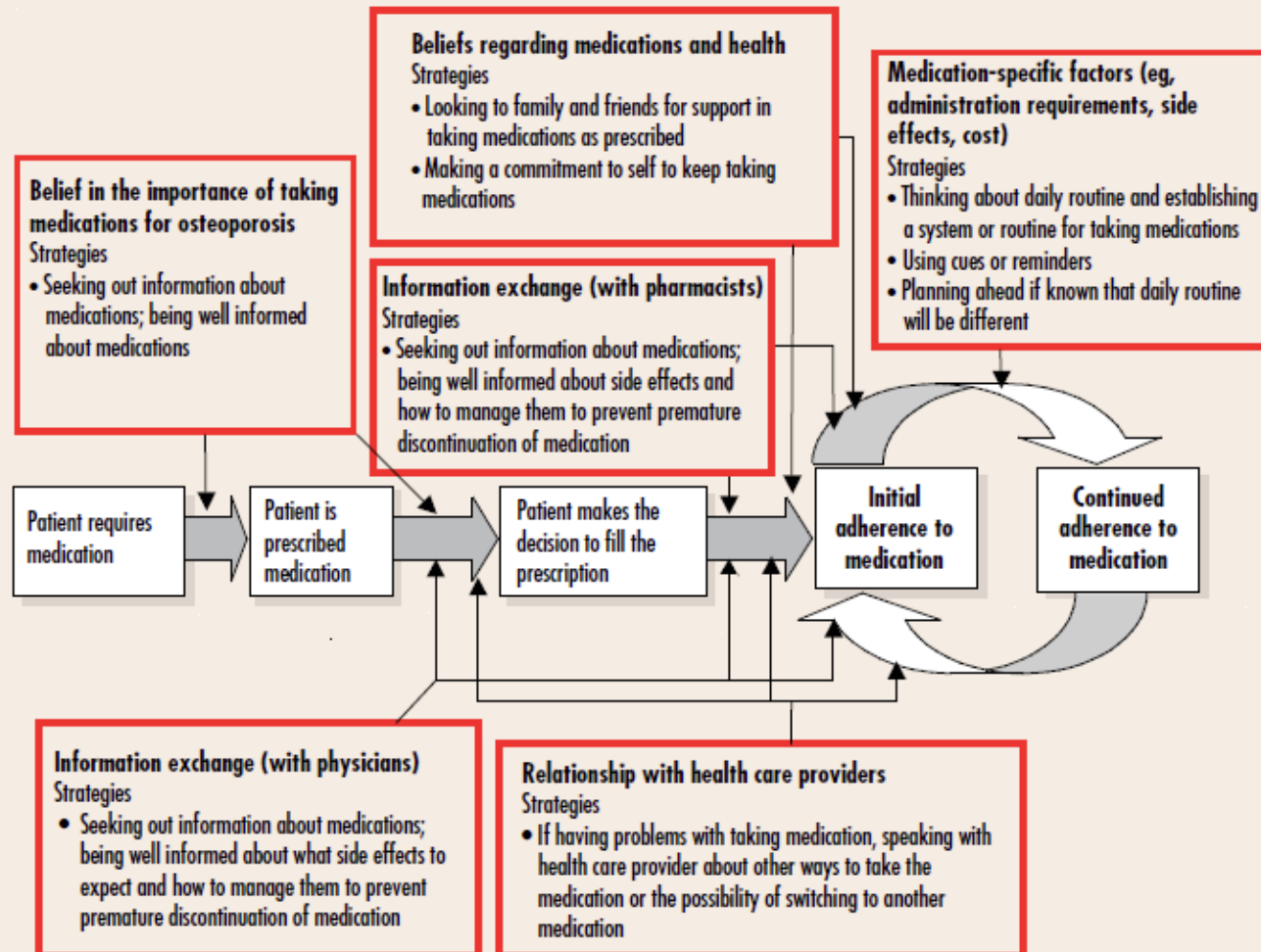
# Solutions: evidence + detective work (by the team)



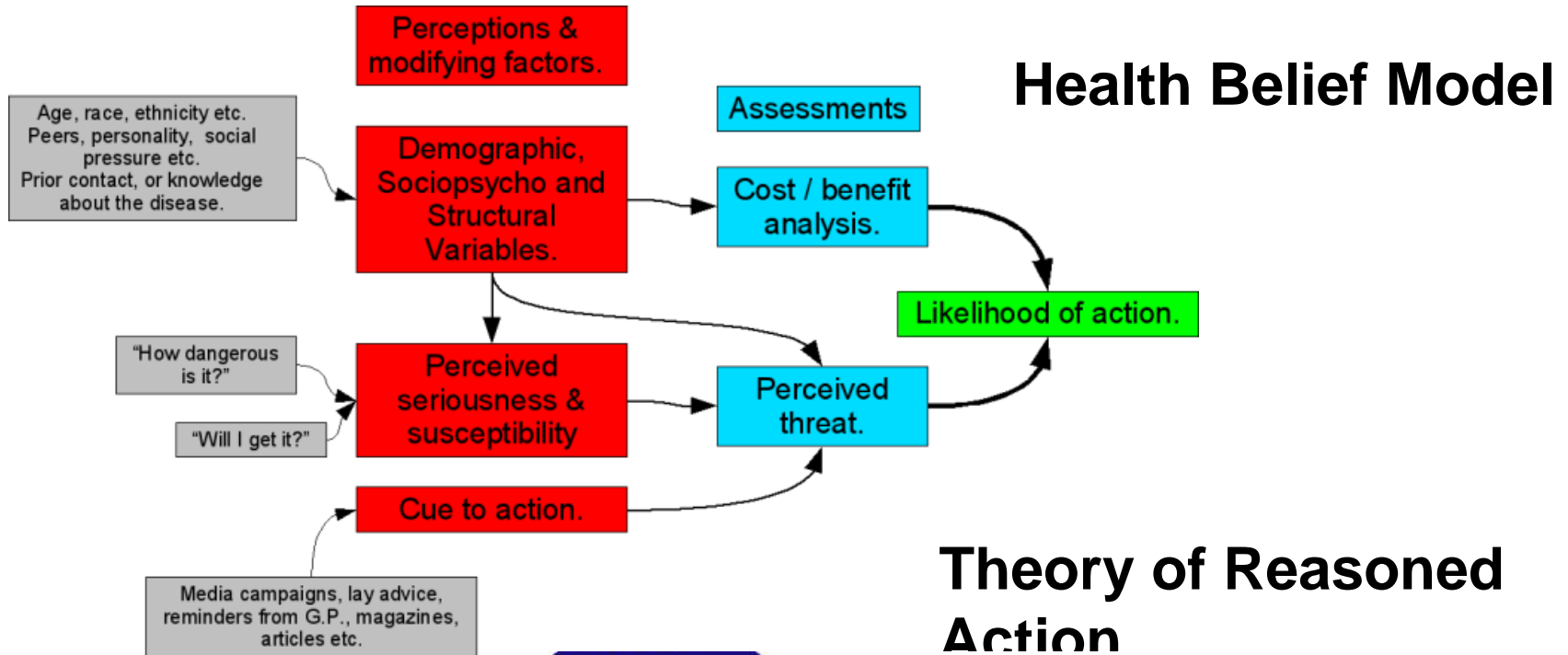
# Focus: on the patient and on the drugs



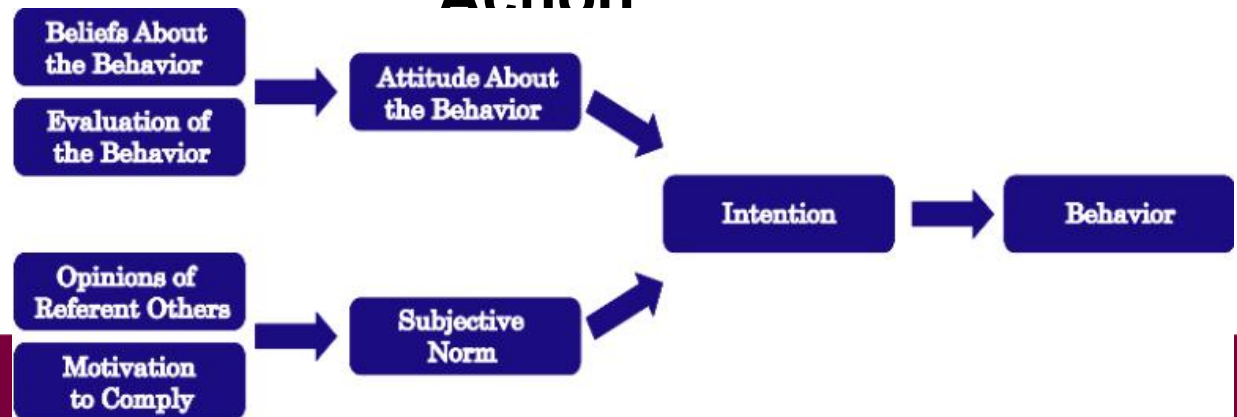
**Figure 1. Mapping the factors influencing adherence and adherence strategies onto the medication-taking process**



# Theories can help understand Non Adherence



## Theory of Reasoned Action



Fishbein-Aizen Theory of Reasoned Action



# Interventions for enhancing medication adherence

(Haynes, RB et al, Cochrane Review, 2008)



- Long-term treatments:
  - 36 of 83 interventions (70 RCTs) associated with improvements in adherence,
  - only 25 interventions: improvement in at least 1 treatment outcome.
- Improve adherence and treatment outcomes by:
  - simplifying the dosage regimen
  - combinations of more thorough instructions and counseling, reminders, close follow-up, supervised self-monitoring, rewards for success, family therapy, couple-focused therapy, psychological therapy, crisis intervention, and manual telephone follow-up.

# Interventions for enhancing medication adherence

(Haynes, RB et al, Cochrane Review, 2008)



- Even the most effective interventions did not lead to large improvements in adherence and treatment outcomes
- More frequent interaction with patients with attention to adherence.
- Most studies assessing successful complex interventions did not assess the separate effects of the components
  - ? are all elements were required.
- No studies examined major clinical endpoints.

# Interventions to improve consumers use of medications: an overview of systematic reviews

(Ryan R, Cochrane 2011)



- N = 37 overviews
- Promising interventions to improve adherence and other key medicines use outcomes (eg adverse events, knowledge):
  - self-monitoring and self-management, simplified dosing and interventions directly involving pharmacists.
- Other strategies showed promise but less consistent effects.
  - Reminders, education combined with self-management skills training, counseling or support, financial incentives, and lay health worker interventions.

# Interventions to improve medication adherence among older adults: a meta-analysis (Conn VS, et al Gerontologist 2009)

N=33 RCTs (43 comparisons)

Age: median **age 67 years** (min 60-max 84)

# of Rx meds: **median 5** (min 2 – max 7) \*reported in n=14

Focus: CVD (n= 14); diabetes (n = 3); arthritis (n = 2);  
cancer (n = 2), other (n=12)

# Interventions to improve medication adherence among older adults: a meta-analysis (Conn VS, et al Gerontologist 2009)

- The median number of medications used for MA measurement was 2.
- 13 studies measured MA for all prescribed medications. 8 studies measured MA only for newly prescribed medications.
- MA was measured various ways (e.g. pill counts, self report, electronic monitoring etc...)
- **Pharmacists** were the most common interventionists (n= 19), followed by physicians (n= 6) and nurses (n = 1).

# Interventions to improve medication adherence among older adults: a meta-analysis

(Conn VS, et al Gerontologist 2009)

- Most interventions were **delivered face-to-face** (n= 26); 10 used the telephone and 1 involved mailed materials.
- A standardized mean difference ES:
  - Adherence was 0.33,  $p < .001$
  - Medication knowledge was = 0.48,  $p < .001$
- Those on **3-5 medications** had larger MA outcomes than those on fewer or more medications.

# Interventions to improve medication adherence among older adults: a meta-analysis

(Conn VS, et al Gerontologist 2009)

**More effective** interventions (larger effect sizes) were those that:

- included medication packaging changes
- dose modification
- directed participants to self monitor symptoms related to medications
- succinct written instructions
- a stimulus to take medication (e.g. electronic device that makes a sound)

# Reminder packaging for improving adherence to self administered long-term medications.

(Mahtani K.R, et al Cochrane, 2011)



- 12 studies, 2196 participants
- (n=6) Reminder packaging increased the percentage of pills taken (mean difference (MD) 11% (95% CI % to 17%))
- (n=2) decreased DBP (MD = -5.89 mmHg (95% CI -6.70 to -5.09;  $P < 0.00001$ ))
- (n=2) No effect on SBP
- (n=2) reduced A1C (MD -0.72; 95% CI -0.83 to -0.60;  $P < 0.00001$ )
- (n=1) reminder packaging aid preferred by patients with low literacy levels.

# Personality and medication non-adherence in older adults

(Jerant A., et al 2011)

- Relationship between 5 personality factors (Conscientiousness, Neuroticism, Agreeableness, Extraversion, and Openness) and Non-Adherence
- Older participants of a six-year (Ginkgo Evaluation of Memory) RCT (n=771, >= 72 yrs)
- **Neuroticism** (enduring tendency to experience negative emotional states): only factor associated with non-adherence
- **Lower cognitive function**: a 1 SD decrease in mental status exam score was associated with a 3.0% (95% CI 0.2 to 5.9) Increase in the probability of non-adherence
- **Each 5 year increment in age** associated with a 6.7% (95% CI, 2.4 to 11.0) greater probability of non-adherence

# Therapeutic Complexity on Adherence to Cardiovascular Medications

(Choudhry, NK, et al 2011)

- Rxed a statin (n = 1,827, 395) or ACEI/ARB (n = 1,480,304) over a 1 year period
- Over 3 months statin users filled 11.4 Rxs for 6.3 different meds, at least 2 prescribers, and 5.0 visits to the pharmacy. Similar for ACEI/ARB.
- Greater prescribing and filling complexity was associated with lower levels of adherence.
- Patients with the least refill consolidation had adherence rates that were 8% lower over the subsequent year than patients with the greatest refill consolidation.

# Improving adherence to lipid lowering drugs (Schedbauer A et al, Cochrane review, 2010)



- N=11 RCTs
- Interventions caused a change in adherence ranging from decrease -3% to increase 25%
- (n=6) **Most promising: patient re-enforcement and reminding** investigated in six trials:
  - 4 showed improved adherent behaviour of statistical significance (absolute increase: 24%, 9%, 8% and 6%).
- Other interventions associated with increased adherence were:
  - **simplification of the drug regimen** (absolute increase 11%), and
  - **patient information and education** (absolute increase 13%).

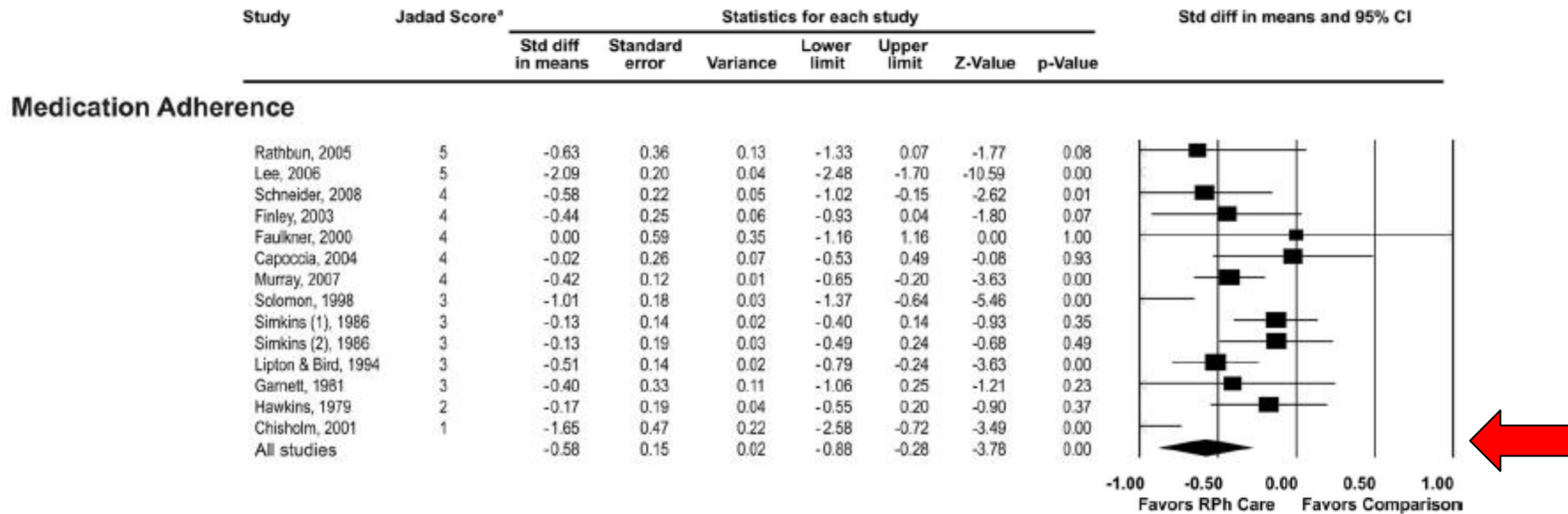
# Pharmacist care: patients with hypertension (Morgado MP, et al 2011)

- N= 15 studies (16 interventions); 3280 patients.
- 87.5% of interventions → improvements in treatment outcomes
- 43.8% of interventions → increases in medication adherence.
- All interventions that increased antihypertensive medication adherence also significantly reduced BP ((SBP) ( $p < 0.001$ ) and diastolic blood pressure (DBP) ( $p = 0.002$ ))
- Effective interventions were complex, including combinations of different strategies.

# Pharmacist care: patients with depression (Rubio-Valera, 2011)

- Six RCTs (n=887 patients)
- Most common interventions:
  - patient education and monitoring, monitoring and management of toxicity and adverse effects, adherence promotion, provision of written or visual information, and recommendation or implementation of changes or adjustments in medication.
- pooled odds ratio demonstrated benefit of pharmacist intervention to increase adherence: 1.64 (95% CI 1.24 to 2.17).

# Pharmacists providing direct patient care (Chisholm-Burns MA et al, 2010)



Standardized mean difference 0.6  
(calculated as the effect size)., p=0.001

# Other considerations supported by evidence

- **Fixed-dose combinations** improve medication compliance (Bangalore S., 2007)
- The estimated odds of a **depressed patient** being nonadherent are 1.76 times the odds of a non-depressed patient, across 31 studies and 18,245 participants. (Grenard J.L, 2011)
- **Drug class** impacts adherence (Kronish IM et al, 2011)
  - pooled mean adherence by drug class ranged from 28% for beta-blockers to 65% for angiotensin II receptor blockers.
- **Stress** is negatively associated with adherence to medication (Watson et al, 2011)
- Higher adherence rates in patients using **less frequently dosed medications** (Saini, SD. Et al, 2009)

# Structured Medication Adherence Assessment

- Encourage patients to share their experience with medications
- Assessing Adherence
  - E g. beliefs and perceptions, physical, emotional, situational, drug regimen
- Try to uncover reasons for non adherence
  - Intentional
  - unintentional

# Solutions:

Focus on the patient and on the drugs

