The Right Balance Between Polypharmacy and Patient Adherence To Care

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Outline

- Overview of polypharmacy and CKD in elderly
- Description of the consequences of polypharmacy
- Prevalence of medication non-adherence
- Factors or perceived barriers to non-adherence
- Approaches to balancing polypharmacy and improve medication adherence

Polypharmacy

Too Many, Too Few…. Getting Medications Just Right

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What is Polypharmacy?

Lack of universally accepted definitions

Taking MANY medications

Definition (numerical threshold)[1,2]:

- Prescribed of four or more medications
- Bought over the counter

[1] Patterson S, et al. Cochrane Database Syst Rev. 2014;10:CD008165

[2] Maher RL, et al. Expert Opin Drug Saf. 2014;13(1):57–65

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Categories of Polypharmacy

Appropriate Polypharmacy

- Prescribing of ‘many drugs’
- Agreed with patients to achieve specific therapeutic goal
- Optimized therapies and minimize the risk of adverse drug reactions (ADRs)

Inappropriate Polypharmacy

- Prescribing of ‘too many’ drugs
- No evidenced indications or expired indications
- Failed to achieve the therapeutic goals
- One or combination of drugs cause inacceptable ADRs or put the patient at high risk of such ADRs

Scottish Government Polypharmacy Model of Care Group. *3rd Edition, 2018*

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Singapore in 2030

25% of population 65 years old and above

Merchant RA, et al. J Am Med Dir Assoc. 2017;18(8):734.e9-734.e14

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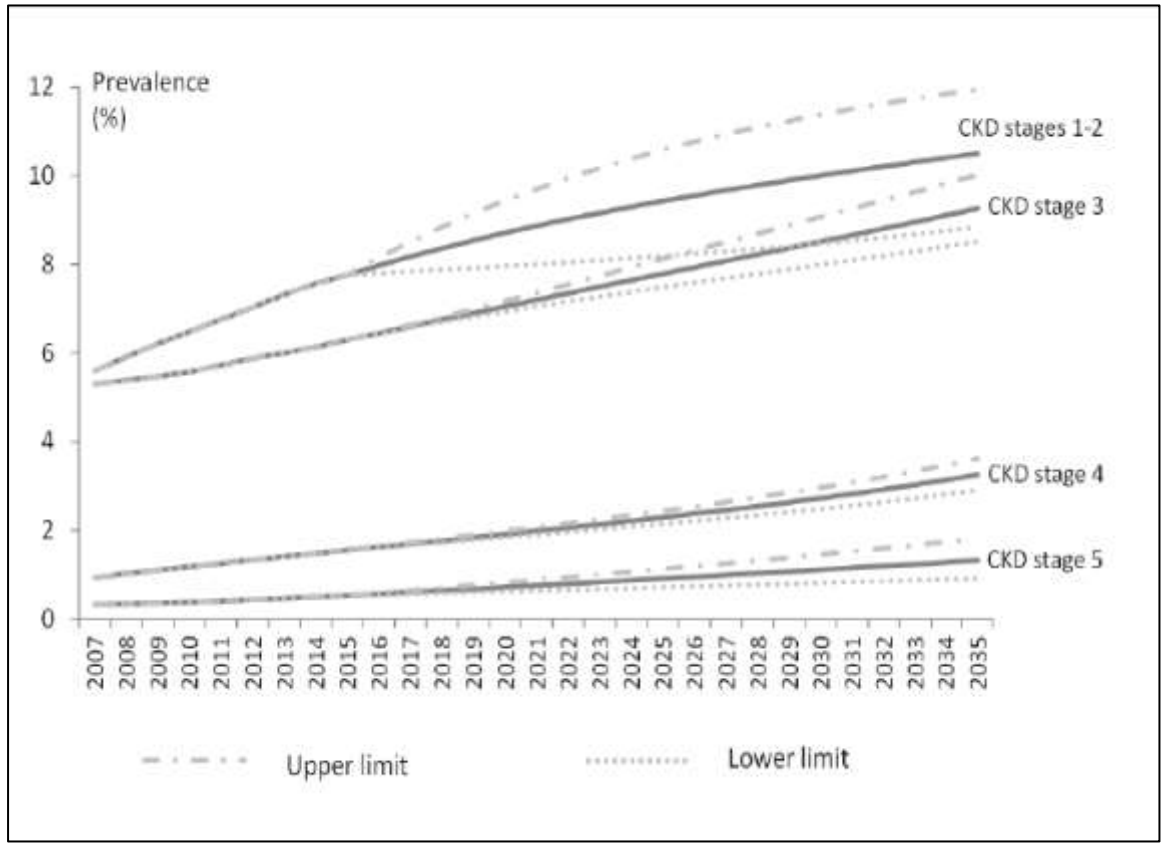
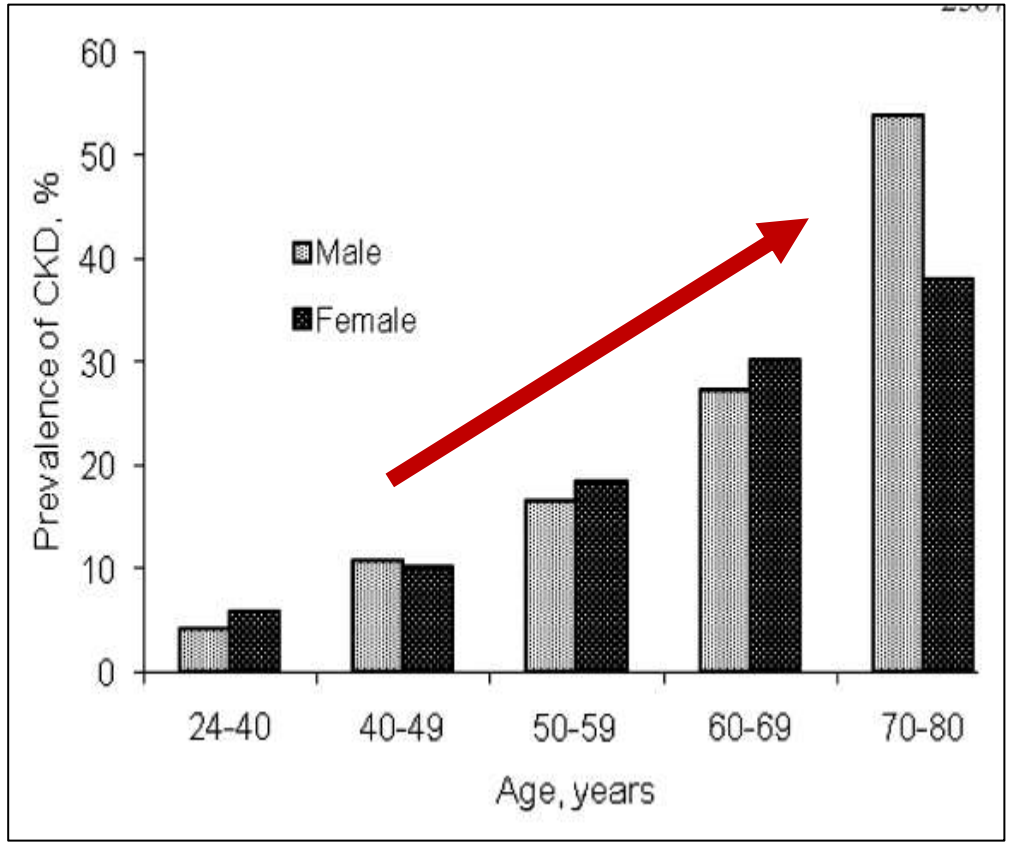
Projection of Singapore residents with CKD using Markov model



By 2035, **~ 24%** of our population was projected to have CKD

Singapore Prospective Study Program



CKD prevalence increased with increasing age

High proportion of CKD patients = Elderly

Sabanayagam C, et al. Nephrol Dial Transplant. 2010;25(8):2564-70

Wong LY, et la. Int J Nephrol. 2018;2018:5196285

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Patient: 86 yo female – CKD S4, T2DM, HTN, HLD

1. SC Recormon 4000 units every 2 weeks
2. Ferbeaplex 2 tabs BD
3. Calcium carbonate 625mg 1 tab TDS
4. Perindopril Erbumine 8 mg 1 tab OM
5. Nifedipine LA 60mg 1 tab BD
6. Furosemide 40mg 1 tab OM
7. Rosuvastatin 10mg 1 tab ON
8. Sodium Bicarbonate 500mg 2 caps BD
9. Glipizide 5mg 1 tab BD
10. Linagliptin 5mg 1 tab OM
11. Mecobalamin 500mg 1 tab OM
12. Colecalciferol 50000 units every month
13. Neurobion 1 tab BD
14. Lactulose 10mL TDS prn
15. Sennosides 7.5mg 2 tabs ON

High burden of pills a day

How many pills are this patient taking daily ?

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Medications	Morning	Noon	Dinner
Ferbeaplex 2 tabs BD			
Calcium carbonate 625mg 1 tab TDS			
Perindopril Erbumine 8 mg 1 tab OM			
Nifedipine LA 60mg 1 tab BD			
Furosemide 40mg 1 tab OM			
Rosuvastatin 10mg 1 tab ON			
Sodium Bicarbonate 500mg 2 caps BD			
Glipizide 5mg 2 tabs BD			
Linagliptin 5mg 1 tab OM			
Mecobalamin 500mg 1 tab OM			
Neurobion 1 tab BD			
Sennosides 7.5mg 2 tabs ON			
26	14	1	11

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Commonly Prescribed Medications in CKD/ESKD

- Antihypertensives/ Cardiovascular
- Glucose Lowering Drugs
- Lipid lowering drugs
- Vitamin D Preparations
- Phosphate Binders
- Calcimimetics
- Iron Supplements
- Erythropoiesis Stimulating agents

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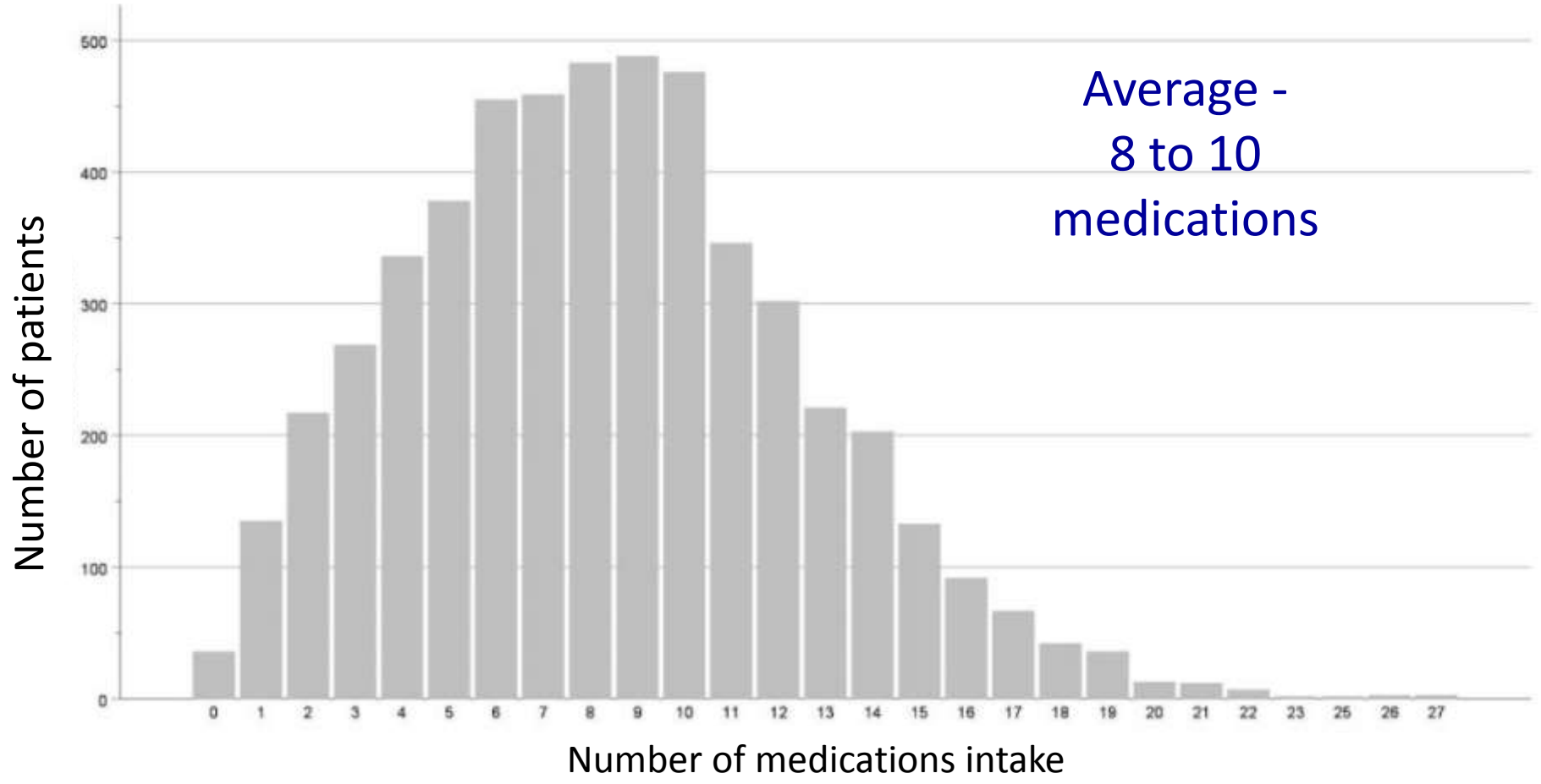
Polypharmacy in CKD



Schmidt IM, et al. Clinical Kidney Journal, 2019. 1-10

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When More is Less …..

Polypharmacy leads to:

- More adverse drug reactions (ADRs) [1]
  - Increased risk by 88% in patients taking 5 or more meds
- **Non-adherence** to drug regimens[2]
  - Associated with disease progression, treatment failure, hospitalization
- Drug-interactions[3]
  - 50% chance when taking 5 – 9 meds
  - 100% chance when taking 20 or more meds
- Adverse patient outcomes[4]
  - Reduced ability to perform instrumental activities of daily living
  - Associated with dementia and delirium
- Increased healthcare cost [4]
  - Increased risk of hospitalizations & emergency department visits
- Falls

[1] Bourgeois FT, et al. Pharmacoepidemio Drug Saf. 2010;19:901-10
[2] Vik SA. Ann. Pharmacother.2004;38:303-12
[3] Doan J, et al. Ann Pharmacother. 2013;47:324-32
[4] Robert L, et al. Expert Opin Drug Saf. 2014;13(1): 57-65

Adherence: Definition

The extent to which an individual's behavior regarding a medical treatment regimen corresponds with the **agreed-upon recommendations** of a healthcare professional (HCP)

Compliance

- Suggest that patients are obeying a HCP

Adherence

- Implies collaboration between HCP and patients

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Prevalence of Medication Non-Adherence

Wide variations:

- Varies from 17 to 74% among patients with CKD [1]
- From 3 – 80% among patients on hemodialysis [1]
- Highly prevalent - 42.5% among hemodialysis patients in SGH [2]

Non-adherence:

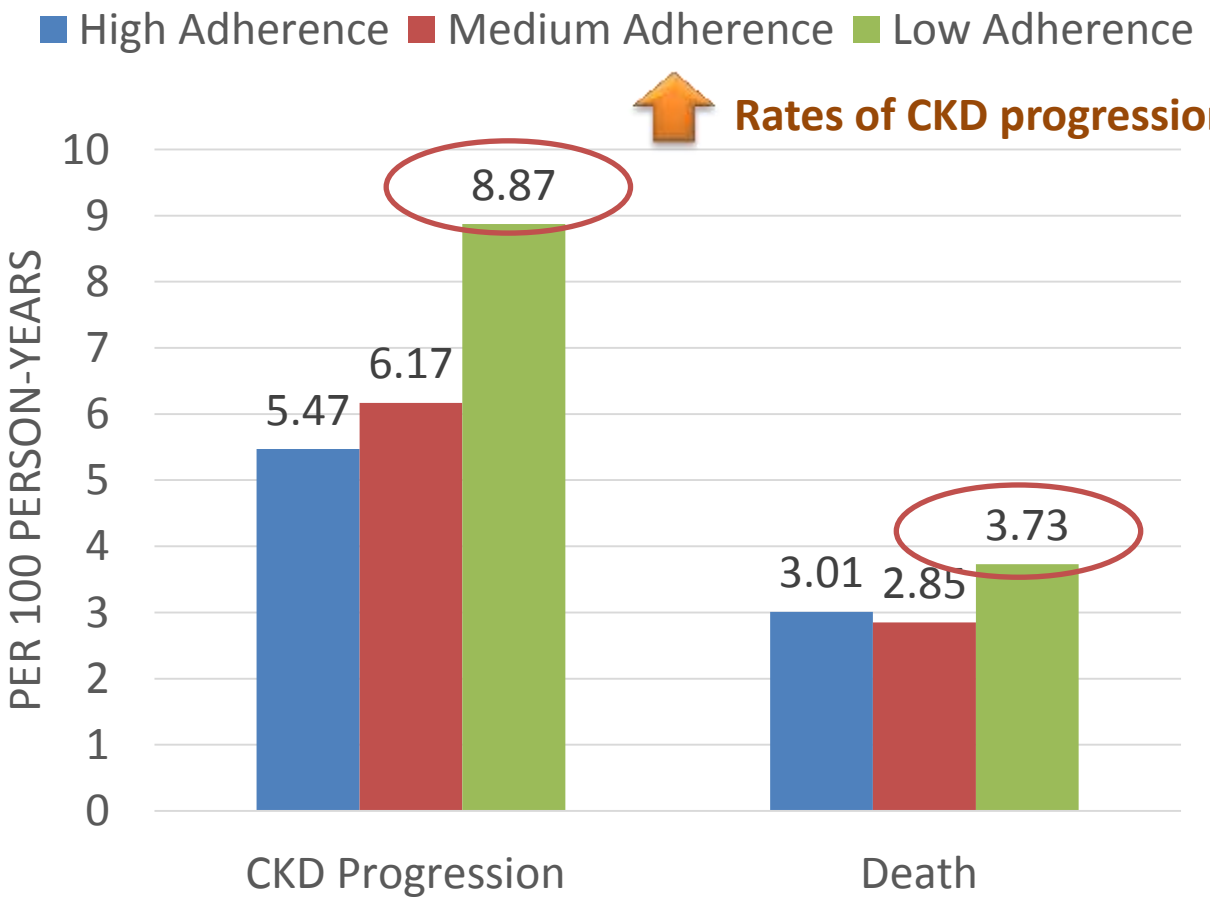
- Phosphate binders[1]: 22 – 74%
- Antihypertensives[2]: Mean 38.5%
- Antidiabetics[2]: Mean 61.2%
- Antidyslipidaemics[2]: Mean 46%

1 Nielsen TM, et al. Clinical Kidney Journal, 2018;11(4):513-527
2 Chia BY, et al. Int J Clin Pharm. 2017;39(5):1031-1038

1 Karamanidou C, et al. BMC Nephrology, 2008;9:2
2 Ghimire S, et al. Plos Obe. 2015;10(12):e0144119

Drugs don't work in patients who don't take them

Rates of CKD progression and all-cause death, by level of med adherence



Association of medication adherence status with CKD progression and all-cause death (n=3305)

Outcome	Predictor of adherence	Adjusted HR 95% CI
CKD progression	High (ref)	1.00
	Medium	1.08 (0.89,1.31)
	Low	1.27 (1.05, 1.54)
Death	High (ref)	1.00
	Medium	0.98 (0.76, 1.28)
	Low	1.14 (0.88, 1.47)

Data are adjusted HR for clinical center, sociodemographic factors, clinical factors, CV medications, no. of types of meds per day and Beck Depression Inventory –II score

Risk of CKD progression by 27%

Cedillo-Couvert EA, et al. Kidney Int Rep. 2018;3(3):645-651

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Drugs don't work in patients who don't take them

- Uncontrolled blood pressure
- Fluid overload
- Rapid progression of CKD
- Worsening of other clinical conditions - cardiovascular disease; diabetes
- Complications of poor disease management
- Increase hospitalizations and emergency department visits
- Increase mortality

} Increase cost burden in health care system

Saran R, et al. Kidney Int 64:254-262

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Factors & Perceived Barriers for Non-adherence

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WHO

WHAT

HOW

WHERE

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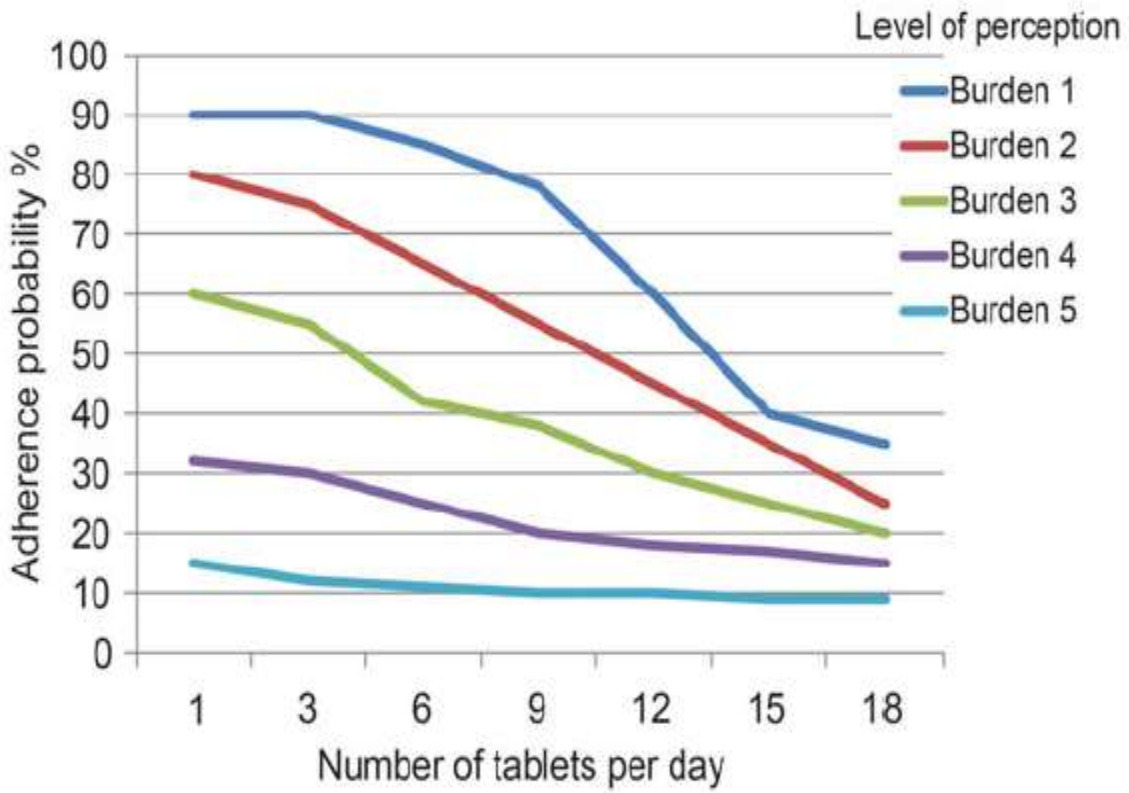
WHO: Patient factors – Most consistently identified predictors of non-adherence



Relationship between the number of tablets per day and the probability of adherence according to the perception of the burden of therapy in dialysis patients

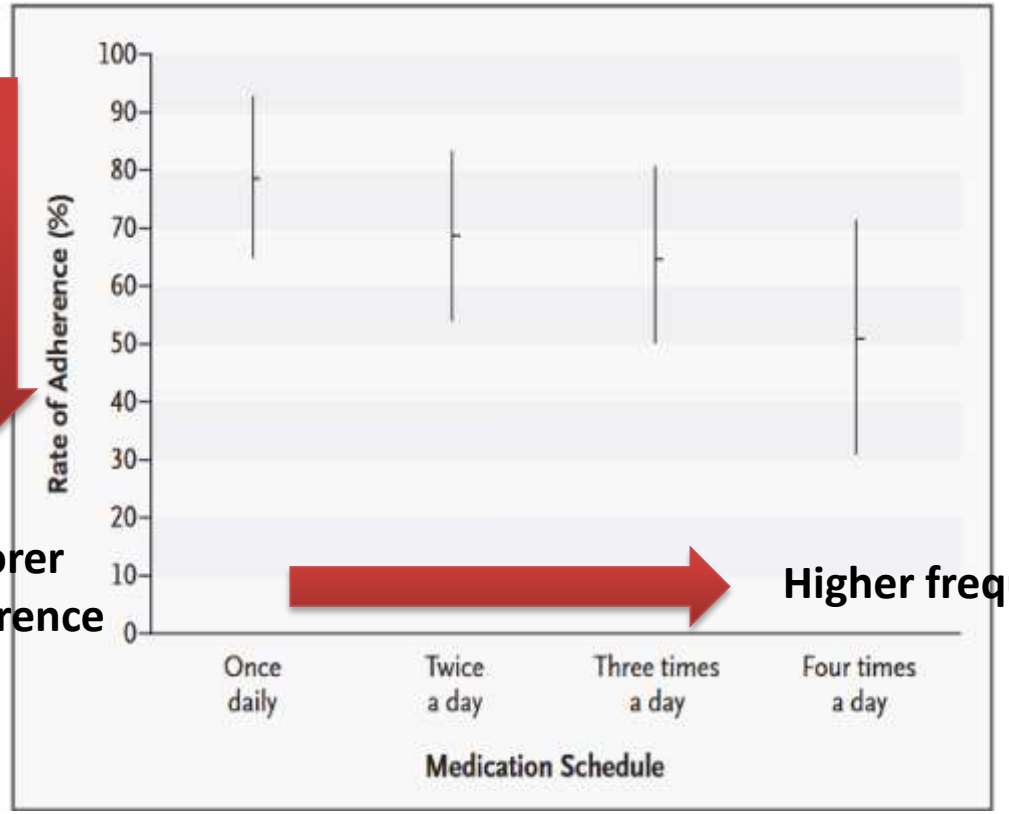
Neri L, et al. Am J Nephrol 2011:34:71-76

- Lacking understanding about medication indication and effects
- Absence of effect from patient perspective
- Concerns about pill burden and pill size
- Poor tolerance or side-effects of meds
- Miscommunication with providers
- Beliefs about medications vs. conventional medical opinion

Reflects a combination of factors

Michel B, et al. Nephrol Dial Transplant (2015)30:39-44
Rifkin DE, et al. Am J Kidney Dis. 2010;56(3):439-46

WHAT: Complex dosing regimens



Poorer Adherence

Higher frequency

Adherence to medication according to frequency of doses

Likely relates to multiple factors:

- Forgetfulness
- Treatment and illness perceptions
- Drug interactions/side -effects

Frequent Dosing

Poorer adherence

Osterberg L, et al. NEJM 2005;353:487-97

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WHAT: Complex dosing regimens

ESKD patient with hemodialysis:

Nifedipine LA 60mg BD on non-dialysis days
Nifedipine LA 30mg BD on dialysis days

Mixtard 20 units pre-breakfast and 10 units pre-dinner on non-dialysis days
Mixtard 10 units BD on dialysis days

Adjusted and tailored to patient's BP and blood glucose.

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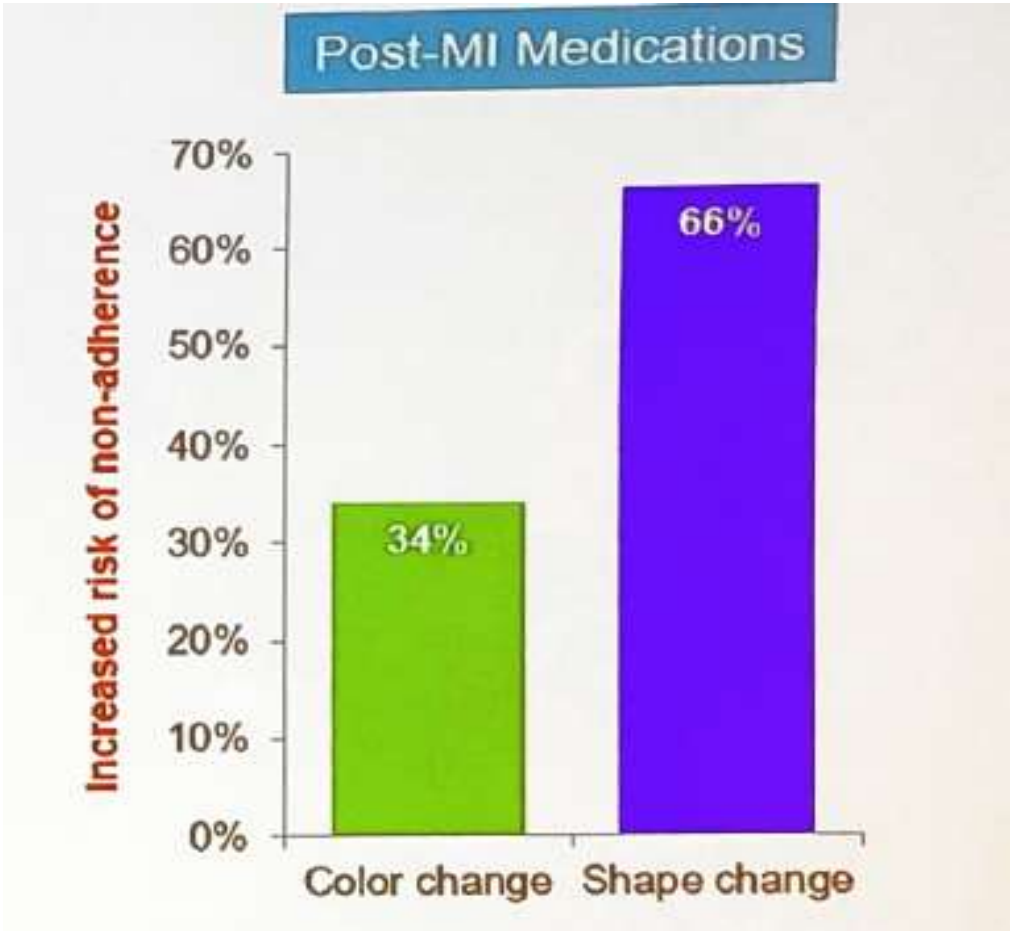
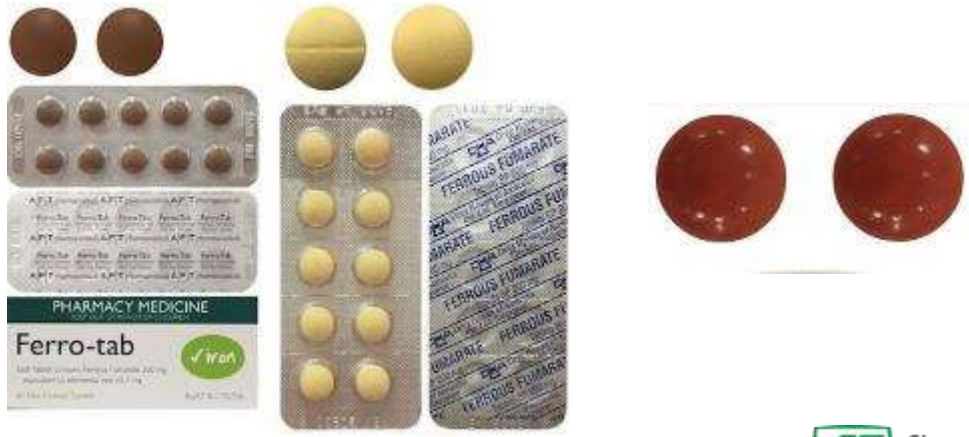
WHAT: Pill Appearance



Kesselheim AS, et al. Ann Intern Med. 2014;161(2):96-103

Calcium acetate: Round or oblong shape



Iron supplement: Brown, yellow, red

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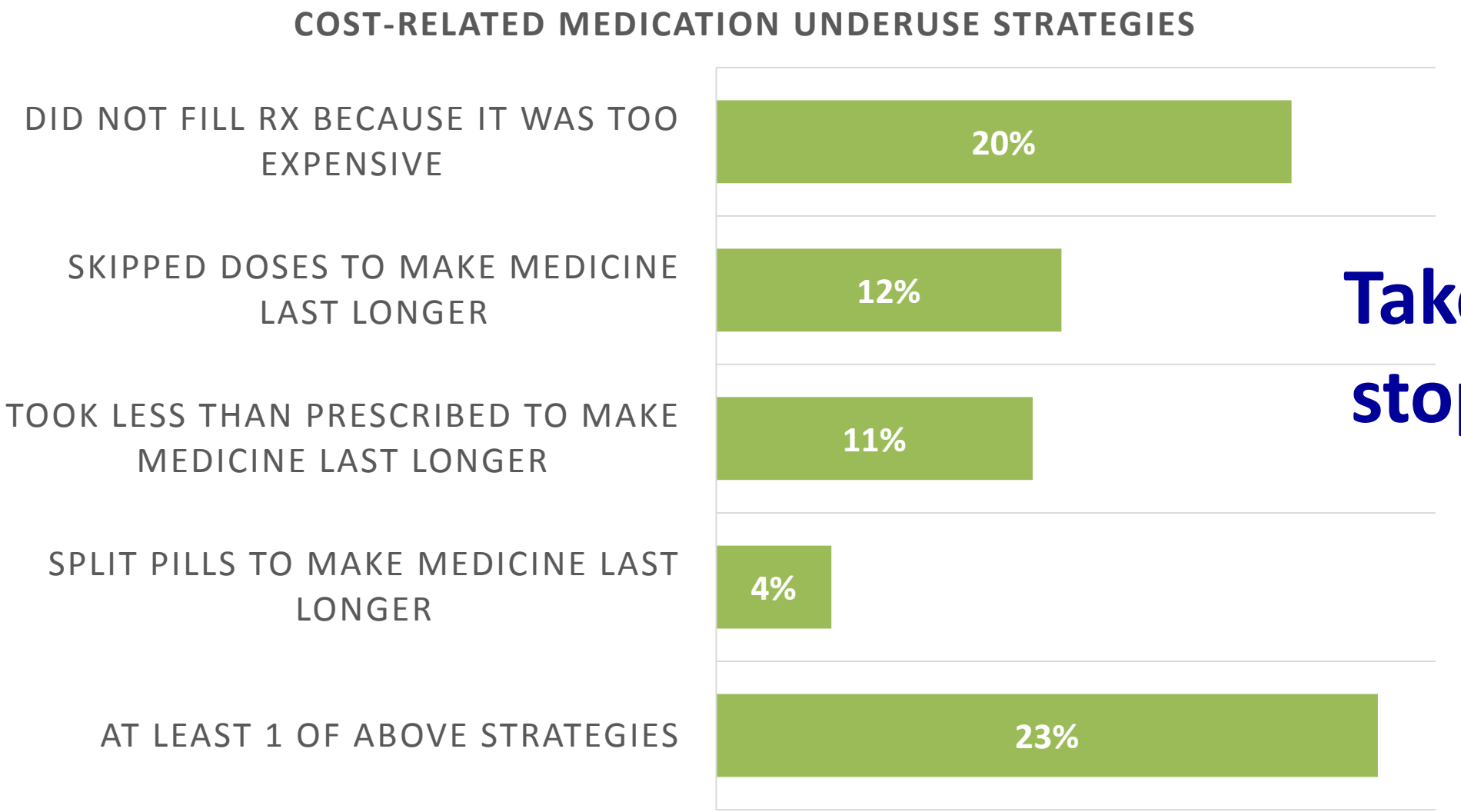
WHAT: Costs – Consistent contributor to non-adherence



Take less or stop taking

Choudhry NK, et al. J.Hosp.Med.2012;7(2):104-109

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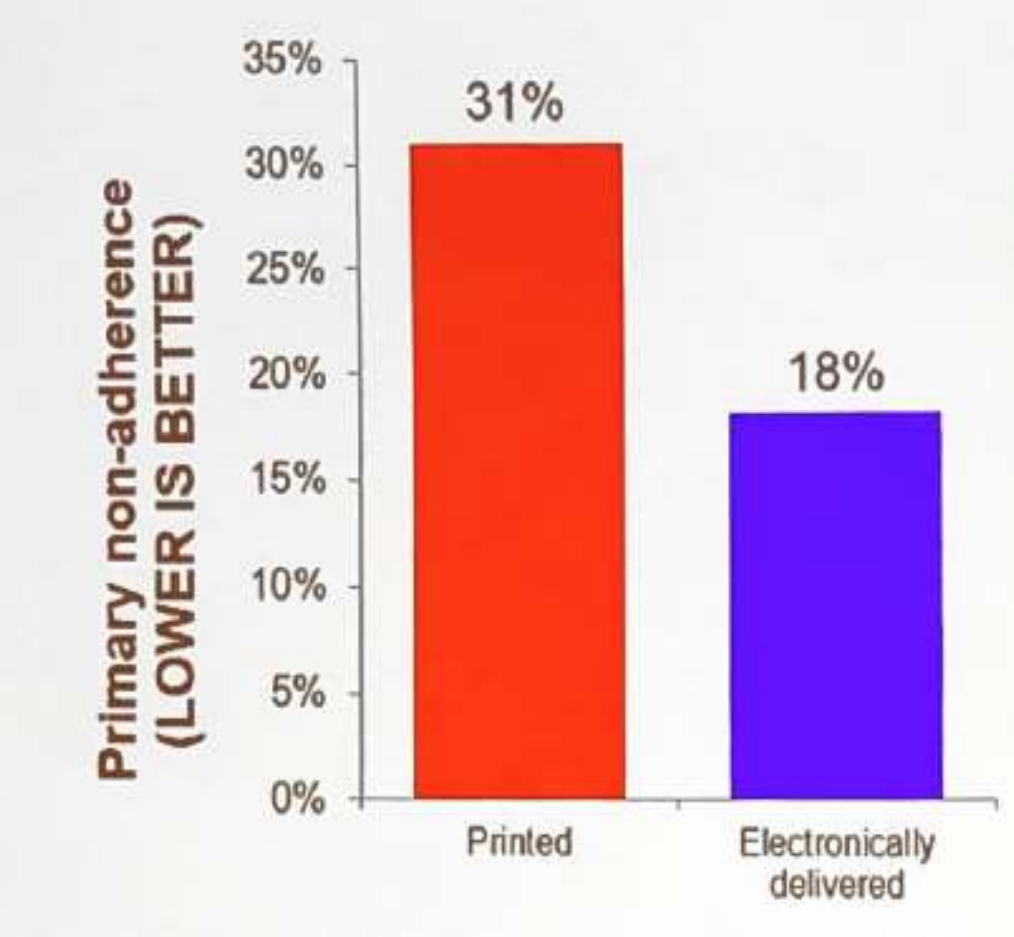
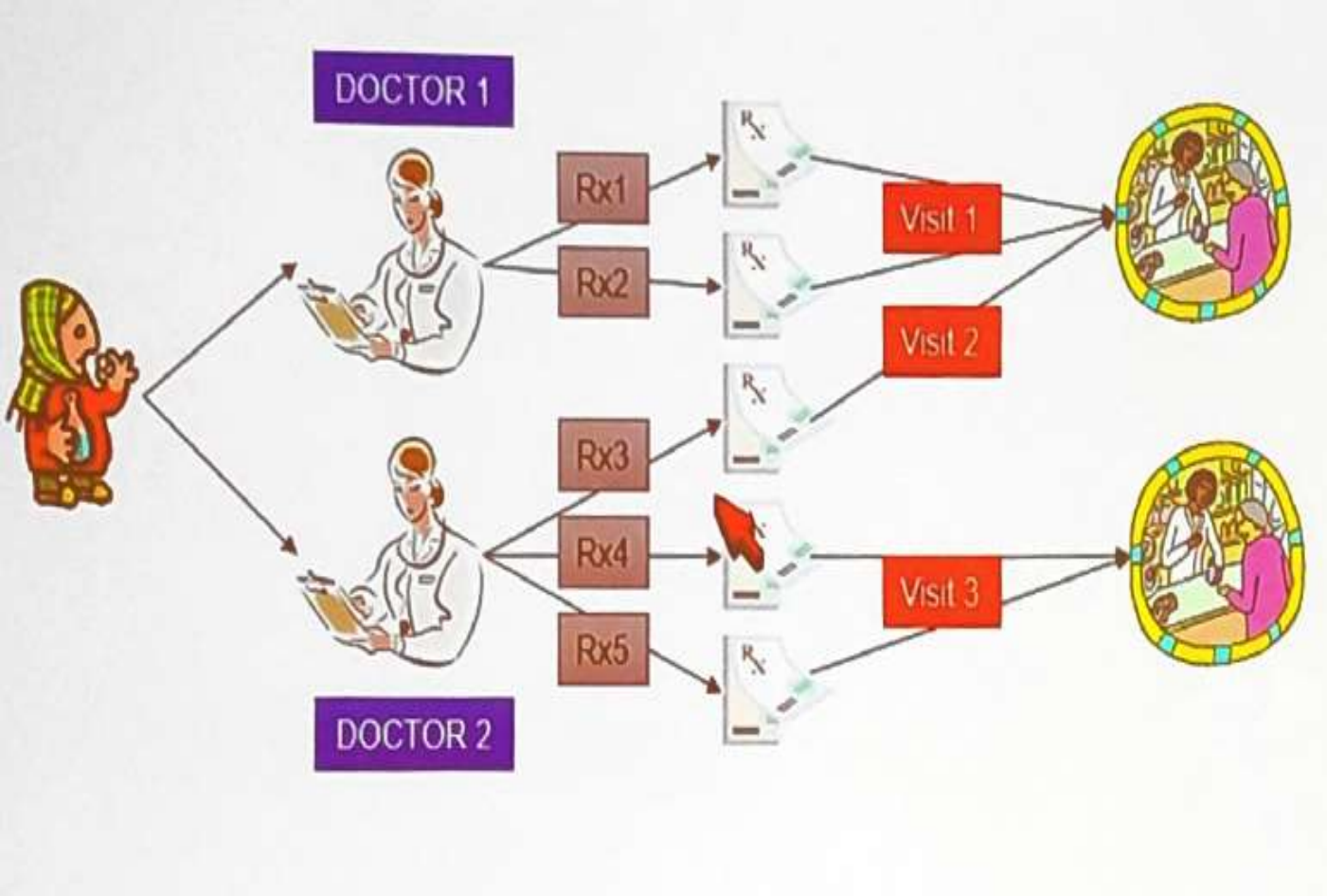
HOW: Printed Rx lead to greater non-adherence



- Primary non-adherence refers to non-adherence to newly prescribed medications
- Higher rates when Rx are printed out and handed to patients vs. delivering them electronically

Fischer MA, et al. Am J Med. 2011;124(11):1081.e9-22

WHERE: Health System Complexity



- Multiple trips to the pharmacy to refill reduces adherence by 8% vs. patients whose refills are most 'consolidated'

Choudhry et al. Archives of Internal Medicine;2011;171:814-822

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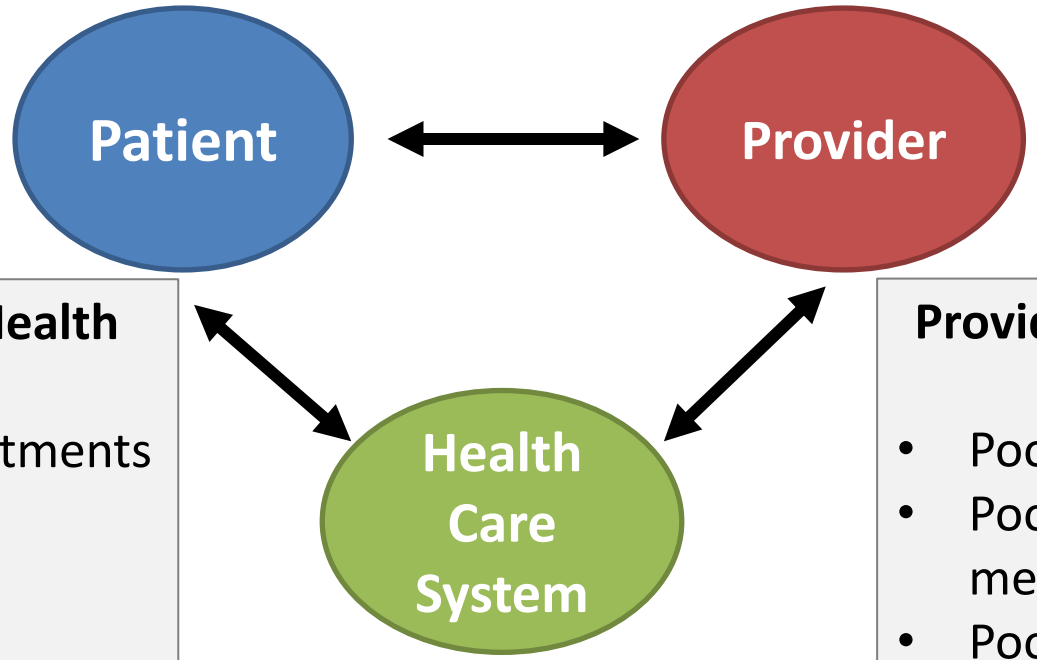
Non-adherence: Complex behavioral issue

Provider-Patient Communication

- Poor patient understanding of disease
- Poor understanding of risks and benefits of treatment
- Poor understanding of use of medication
- Overly complex drug regimen



Patients Interaction with the Health Care System

- Poor access or missed appointments
- Poor access to medications
- Switching formularies
- High cost medications

Provider's Interaction with the Health Care System

- Poor knowledge of drug costs
- Poor knowledge of insurance or medisave coverage of formularies
- Poor job satisfaction

Osterberg L, et al. NEJM 2005;353:487-97

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Non-adherence

Is a two-way street !

Work in partnership with patients

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There's got to be a happy medium – To improve adherence

Quality of Provider – Patient relationships

- Collaborative -> develop trust and give motivation
- Well-informed & involved in decisions concerning meds
- Provide adequate information for the prescribed meds
- Consider the side-effects experienced by patient

Collaborative approach

1. **Medication review**
2. **Optimize control rates**
3. **Counseling**

- Discrepancy btw patient actual vs. prescribed dosing
- Brown bag snapshots or home visits
- Involvement of specialized nurses or pharmacists to enhance the control rates of various risk factors
- Medications and disease management counseling – support patients in coping with side-effects

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Medications & Non-Pharmacological Counseling

High Serum Phosphate

Continue adding more tablets or
New phosphate binders

Vs.

Avoid food rich in
phosphorus

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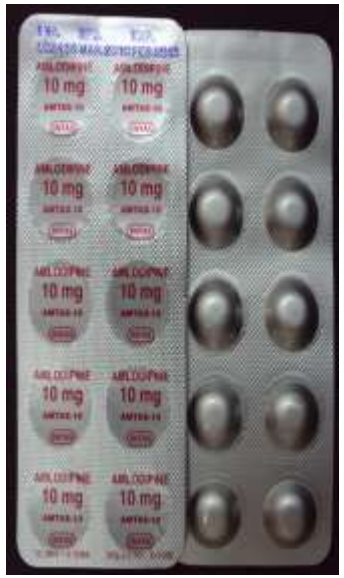
Medications & Non-Pharmacological Counseling

High Blood Pressure



Continue adding more tablets or
New antihypertensive drugs

Vs.

Control **fluids** (daily allowance)
and reduce **salt** intake

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Evaluating Drug Therapies – To improve adherence

Simplify Drug Regimens

Daily vs. frequent dosing

Enalapril BD dosing

vs.

Losartan daily dosing

Oral vs. IV formulation in HD patient (increased cost)

Daily oral iron (Ferbeaplex®)

vs.

Monthly or weekly IV iron (Venofer®)

Increased cost!

De-prescribing

- Started PPI while work up CKD anemia (not on Antiplatelet/anticoagulant)
- PRN medications or multiple supplements eg: Renalvite + neurobion
- Continuation of furosemide in HD patients ?

Strategies – To improve adherence

- Identify poor adherence
  - Lack of response to medications
  - Missed appointments
  - Missed refills
- Emphasize the importance/value of the regimen and the effect of adherence
- Elicit patient's ability to follow the regimen and design supports to promote adherence
- Provide simple, clear instructions and simplify regimen
- Obtain the help from family members and community services when needed
- Reinforce desirable behavior and results when appropriate
- Encourage the use of a medication-taking system

Other numerous ways to improve adherence

Informational

Cognitive strategies designed to educate and motivate patients by instructional means

Behavioral

Influence behavior through shaping, reminding, or rewarding desired behavior

Family & Social

Social support strategies, whether provided by family or another group

Kripalani et al. Archives Internal Medicine 2007; 167:540-440

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Most promising appear to be ….

Reduced out - of pocket costs

Case management

Patient educational materials

Reminders

Multicomponent interventions

Many factors contributing to medication non-adherence

→ Need multifactorial approach

Viswanathan et al. Ann Intern Med 2012;157:785-795

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Take Points

- Polypharmacy is prevalent across the spectrum of CKD patients
- Medication non-adherence is a central contributor to suboptimal outcomes in patients with chronic disease
- Non-adherence is a multi-faceted and complex behavioral process
- Wide variety of strategies to address adherence but there is still much work to do!
- Health care professional play an important role in influencing patients' medication adherence

When Many Is Not Too Many….

Thank you

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