MEASURING ADHERENCE AND PERSISTENCE

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Methods to Measure. Adherence & Persistence

- Single Measures:
  - Surveys including self-report of medication utilization using standardized, validated, patient administered questionnaires (e.g. Morisky Scale, Brief Medication Questionnaire, Health Belief Model Questionnaire, Medication Adherence Rating Scale). Overestimates adherence, unreliable
  - Pill counts: counting remaining dosage units (e.g. tablets). Timing of dosage and patterns of missed dosages are not captured using this strategy. Overestimate adherence, time consuming
  - Biochemical measurement of drugs or metabolites in blood or urine. Not available for all medications, expensive and time consuming

Curr Med Res Opin. 2018 May 17:1-27.

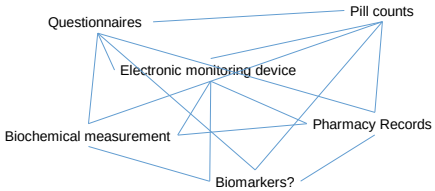
Methods to Measure. Adherence & Persistence

- Single Measures:
  - Electronic monitoring device, e.g. Medication event monitoring systems (MEMS), which records the time and date when a medication container is opened. Expensive, unrealistic for clinical practice
  - Refill data or pharmacy records to check when prescriptions are initially filled, refilled over time, and prematurely discontinued. Unrealistic for clinical practice.

Curr Med Res Opin. 2018 May 17:1-27.

Methods to Measure Adherence & Persistence

- Multiple Measures



Curr Med Res Opin. 2018 May 17:1-27.

Exercise
Understanding Measures of Adherence

- In 5 groups of 2-3 participants each, please discuss what are the pros/cons of the method assigned to your team.

Team	Pros& Cons of:
	Surveys
	Pill counts
	Biochemical measure
	Electronic monitoring device
	Pharmacy records

Medication Adherence Measurement using Large Databases

- Proportion of days covered (PDC): proportion of days supplied over a specified time period.
  - Days supplied by each prescription fill prospectively populated each day in the array with a value of 1 to indicate that medication is available that day or 0 to indicate no availability. Overlapping days supplied are credited forward to the day with the next 0. The days supplied for the last prescription fill within the observation period is truncated, and the maximum PDC is limited to 1.000 (100%).
- Medication possession ratio (MPR)= # of doses dispensed/dispensing period
  - Sum of days supplied for each prescription dispensed between the date of discharge and 360 days following discharge, divided by 360 days. The days supplied for the last fill before the end of the observation period is truncated by the number of days between the fill and the last day of the study period. The maximum MPR is limited to 1.000 (100%).
- Percentage of adherence = #doses taking / #doses prescribed

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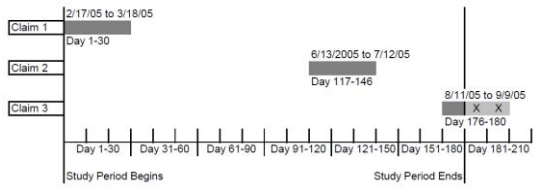
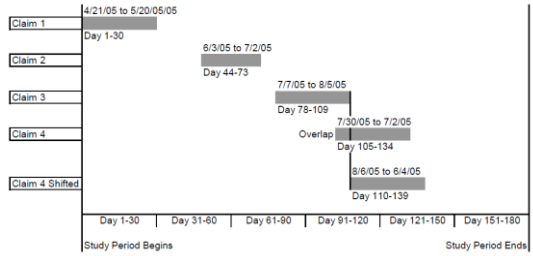
Medication Coverage for 180 Day Period



Leslie S, SAS Forum 2007

Medication Coverage with Overlapping Days Supply



Leslie S, SAS Forum 2007

A systematic literature review comparing methods for the measurement of patient persistence and adherence.

Forbes CA, Deshpande S, Sorio-Vilela F, et al.

- To compare different approaches estimating persistence and adherence in chronic diseases with polypharmacy of oral and subcutaneous treatments.
- Twelve electronic databases and grey literature sources were used to identify studies and guidelines for persistence and adherence of oral and subcutaneous therapies in hypercholesterolemia, type 2 diabetes, hypertension, osteoporosis and rheumatoid arthritis. Outcomes of interest included pros: accurate, easy to use, inexpensive, and cons: inaccurate, difficult to use, expensive of each persistence and adherence data collection and calculation method.
- 4,158 records were retrieved up to March 2017. We included 16 observational studies, 5 systematic reviews and 7 guidelines, in patients with hypercholesterolemia (n = 8), type 2 diabetes (n = 4), hypertension (n = 2), rheumatoid arthritis (n = 1) and mixed patient populations (n = 13).
- Pharmacy and medical records offer accurate, easy and inexpensive data collection method. Pill count, Medication Event Monitoring Systems (MEMs), self-report questionnaires and observer report are easy to use. MEMS and biochemical monitoring tests can be expensive. Proportion of days covered (PDC) was recommended as a gold standard calculation method for long-term treatments.
- The adherence method to use should be based on: route of medication administration, available resources, setting and aim of the assessment. Combining different methods may provide wider insights into adherence and persistence, including patient behaviour.

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Example: Refill-Based Medication Use Quality Measures in Kidney Transplant Recipients: Examination of Proportion of Days Covered and Medication Possession Ratio.

Hofmeyer BA, Look KA, Hager DR.

- To describe the frequency distribution of MPR and PDC using mycophenolic acid products in a real-world kidney transplant recipient population and evaluate associations between MPR and PDC with late (> 90 days after transplantation) **biopsy-proven acute rejection (BPAR).**
- Retrospective cohort study from the **Wisconsin Allograft Recipient Database with University of Wisconsin (UW) Health Specialty Pharmacy prescription claims and dispensing data** from March 10, **2006**, to June 30, **2012**. Patients who met criteria for persistence filling mycophenolic acid prescriptions at UW Health Specialty Pharmacy in the first year following discharge from kidney transplantation surgery hospitalization were included. Patients were excluded if they were enrolled in a clinical trial, if they had BPAR within 90 days of transplantation, or if they did not have panel reactive antibody data available.
- PDC and MPR were calculated over 360 days after discharge, PDC or MPR associations with late BPAR within 3 years were estimated using multivariate analyses.
- N=388 patients. The incidence of 3-year late BPAR was 5.1% (n = 20). Number of hospital readmissions was higher among patients who experienced late BPAR. The median **PDC= 0.972,** median MPR of 1.000. **Higher PDC was associated with lower odds of late BPAR (OR = 0.041, 95% CI = 0.004-0.417), as was a higher MPR (OR = 0.041, 95% CI = 0.004-0.419).**
- MPR and PDC may be calculated from data available to pharmacies and health plans, and each was associated with 3-year late BPAR among patients who did not experience early BPAR.

J Manag Care Spec Pharm. 2018 Apr;24(4):367-372

Multivariable Analyses of BPAR with MPR or PDC in Model

Variable (Comparator)	Adjusted MPR Model c-statistic: 0.780		Adjusted PDC Model c-statistic: 0.776	
	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
MPR or PDC, continuous	0.041 (0.004–0.419)	< 0.007	0.041 (0.004–0.417)	< 0.007
Age, continuous	1.000 (0.965–1.037)	0.978	1.000 (0.965–1.036)	0.981
Female (male)	0.610 (0.215–1.731)	0.353	0.593 (0.208–1.686)	0.327
Black (white) race	1.168 (0.239–5.720)	0.848	1.160 (0.236–5.680)	0.885
Other (white) race	2.481 (0.604–10.202)	0.208	2.552 (0.622–10.480)	0.194
Diabetes (other) primary kidney disease	0.426 (0.088–2.070)	0.290	0.433 (0.089–2.103)	0.299
Prior transplantations count, continuous	0.793 (0.242–2.603)	0.703	0.791 (0.241–2.601)	0.700
Brain death (living) donor	1.130 (0.384–3.322)	0.824	1.111 (0.379–3.255)	0.848
Cardiac death (living) donor	0.380 (0.081–1.771)	0.217	0.377 (0.081–1.762)	0.215
Panel reactive antibodies %, continuous	1.005 (0.973–1.039)	0.746	1.006 (0.974–1.039)	0.718
Hospital readmissions count, continuous	1.502 (1.071–2.106)	0.018	1.502 (1.071–2.105)	0.018

CI = confidence interval; BPAR = biopsy-proven acute rejection; MPR = medication possession ratio; OR = odds ratio; PDC = proportion of days covered.

J Manag Care Spec Pharm. 2018 Apr;24(4):367-372

Measures of Persistence

- Time between refills
- Number of refills (% refills)
- Number of days taking the medication
- Number of gaps (# days with gaps)
- Renewal of prescription with an allowance for a pre-specified gap
- Proportion of patients dispensed a certain number of days' supply of medication
- Proportion of patients continuing to refill prescriptions after a specified time interval

White TJ, Chang E, Leslie S, et al. Patient adherence with HMG reductase inhibitor therapy among users of two types of prescription services. J Manag Care Pharm 2002;8:186–91. Mauskopf JA, Paramore C, Lee WC, Snyder EH. Drug persistency patterns for patients treated with rivastigmine or donepezil in usual care settings. J Manag Care Pharm 2005;11:231–9. Grant RW, O'Leary KM, Wellburg JB, et al. Impact of concurrent medication use on statin adherence and refill persistence. Arch Intern Med 2004;164: 2343–8.

Measuring Persistence

Number of gaps?

ID	D-1	D-30	D-60	D-90	D-120	D-150	D-180	D-210	D-240	D-270	Persistence *# refills=%*
1	X	X			X	X	X		X	X	7=70%
2	X	X	X	X	X	X	X	X	X	X	10=100%
3	X			X			X			X	4=40%
4		X								X	2=20%
5			X		X		X		X	X	5=50%
6	X			X				X		X	4=40%
7			X								1=10%
8	X		X		X		X			X	5=50%
9	X				X					X	3=30%

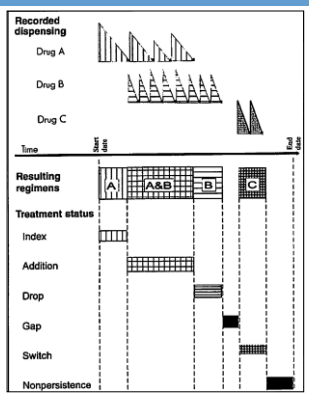
Number of days taking the medication?

Persistence with Treatment for Hypertension in Actual Practice.

Caro JJ, Salas M, Speckman JL, Raggio G, Jackson JD

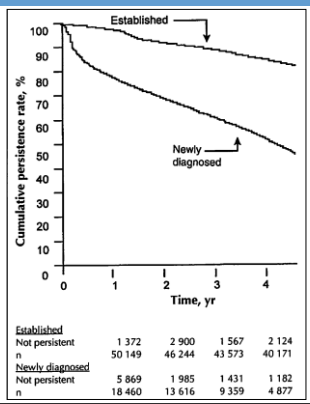
- Cohort study of patients with diagnosis of hypertension, treated between 1989 and 1994 and included in the Saskatchewan Health databases. Patients with concurrent diagnoses likely to affect initial treatment choice were excluded.
- There were 79,591 subjects grouped into those with established hypertension (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.



Drug Regimen Reconstruction and Definition of Changes Illustrated for a Hypothetical Patient

CMAJ, 1999; 160(1)



Cumulative Rate of Persistence with Antihypertensive Therapy for the 2 Groups

CMAJ, 1999; 160(1)

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

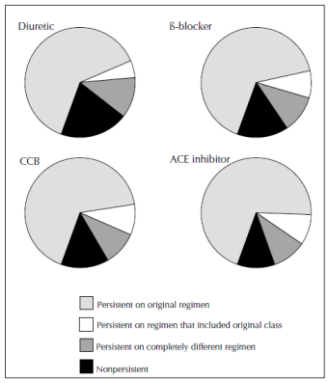
Characteristic	Group; odds ratio (and 95% confidence interval) All patients *n = 74 181*	Patients with newly diagnosed hypertension *n = 22 875*
Established hypertension	10.73 (10.01–11.49)	–
Female sex	1.16 (1.10–1.23)	1.10 (1.03–1.18)
Age ≥ 60 yr	1.11 (1.05–1.18)	1.08 (1.01–1.16)
Hospital admission	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

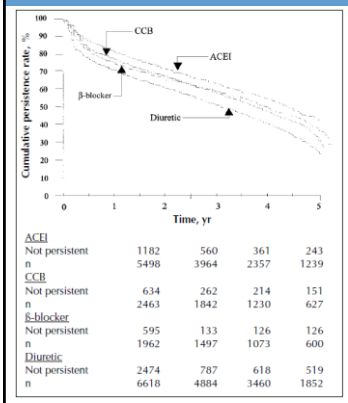
- Using the Saskatchewan database, all outpatient prescriptions for antihypertensive medications filled between 1989 and 1994 were analyzed.
- 22,000 patients with newly diagnosed hypertension whose initial treatment was with a diuretic, beta-blocker, calcium-channel blocker or angiotensin-converting-enzyme (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.



Distribution of antihypertensive regimens by class of index drug after 6 months of therapy for patients with newly diagnosed hypertension in Saskatchewan in 1989–1994

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



ACEI				
Not persistent	1182	560	361	243
n	5498	3964	2357	1239
CCB				
Not persistent	634	262	214	151
n	2463	1842	1230	627
ß-blocker				
Not persistent	595	133	126	126
n	1962	1497	1073	600
Diuretic				
Not persistent	2474	787	618	519
n	6618	4884	3460	1852

Cumulative Rate of Persistence with Antihypertensive Therapy by Index Drug Class

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

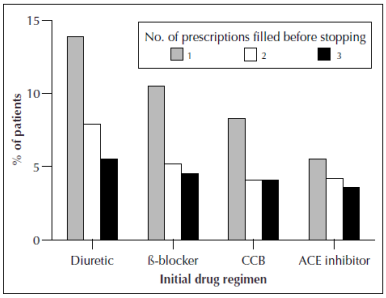
Odds ratio of persistence with antihypertensive therapy through the first year compared with patients who initially received diuretics

Initial drug class	Odds ratio (and 95% confidence interval) Crude	Adjusted*
β-blocker	1.18 (1.06–1.31)	1.25 (1.12–1.39)
CCB	1.45 (1.30–1.61)	1.51 (1.36–1.69)
ACE inhibitor	1.82 (1.67–1.98)	1.92 (1.76–2.09) ←

*Adjusted for age (< 60 yr, or ≥ 60 yr), sex and, in the previous year, the number of physician visits (< 8, or ≥ 8), hospital admissions (none, or ≥ 1) and prescriptions for medications other than antihypertensive agents (< 4, or ≥ 4).

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

Proportion of Patients who Stopped Antihypertensive Treatment Before Filling 4 Prescriptions, by Index Drug Class



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

In Conclusion…