



The Culture and Science of Polypharmacy

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Concerned Citizen, Curious Colleague

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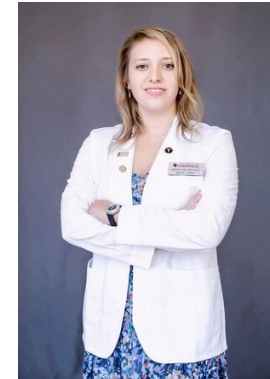
Consultant Pharmacist; Long Term Care & Assisted Living Care



Basic Science Learners



Research Interests:
Decision Making Re Medication Use



Clinical Learners

- Consumers
- Patients
- Caregivers
- Physicians
- Nurses
- Pharmacist
- PT, OT, RT
- Hidden impact of polypharmacy

The “hidden” impact of polypharmacy



What is Polypharmacy?



- 5 or more medications taken simultaneously

- More medications used than are clinically warranted.

- A Random Uncontrolled Experiment

• Types of Polypharmacy

- Too many drugs
- Inappropriate choices
- Inappropriate combinations
- Administration errors
- Way off label use
- Inappropriate dosing
- Inappropriate prescriber

Polypharmacy: A Silent Epidemic



(she looks fuzzy because she's in the "fog")

A side effect of modern medical care

- 15-minute office visit/Hospital visit
- Cornerstone of guideline driven care (GDC)
 - “lifestyle changes, and if LC ineffective”
 - X
 - Y
 - Z
 - GC derived mostly from clinical drug studies (CDS)
 - CDS are efficacy trials against placebo
 - Set up for consumerism not necessarily for superior intervention discovery
 - Example: current dementia treatments
- New drugs added annually and marketed direct .
- Multiple specialists
- Over the counter products and supplements proliferation

Polypharmacy: A Silent Epidemic

106,000; medication
related problems*



* A conservative
(very) estimate

United States Annual Causes of Death	
All causes	2,712,630
1. Heart Disease	633,842
2. Cancer	595,930
3. Lower Respiratory Disease	155,041
4. Accidents	146,571
5. Cerebral Vascular Disease	140,323
6. Alzheimer's Disease	110,561
7. Diabetes Mellitus	79,535
8. Influenza and Pneumonia	57,062
9. Nephritis	49,959

Errors leading to ADEs in ambulatory older adults (mean age 75): 65-80

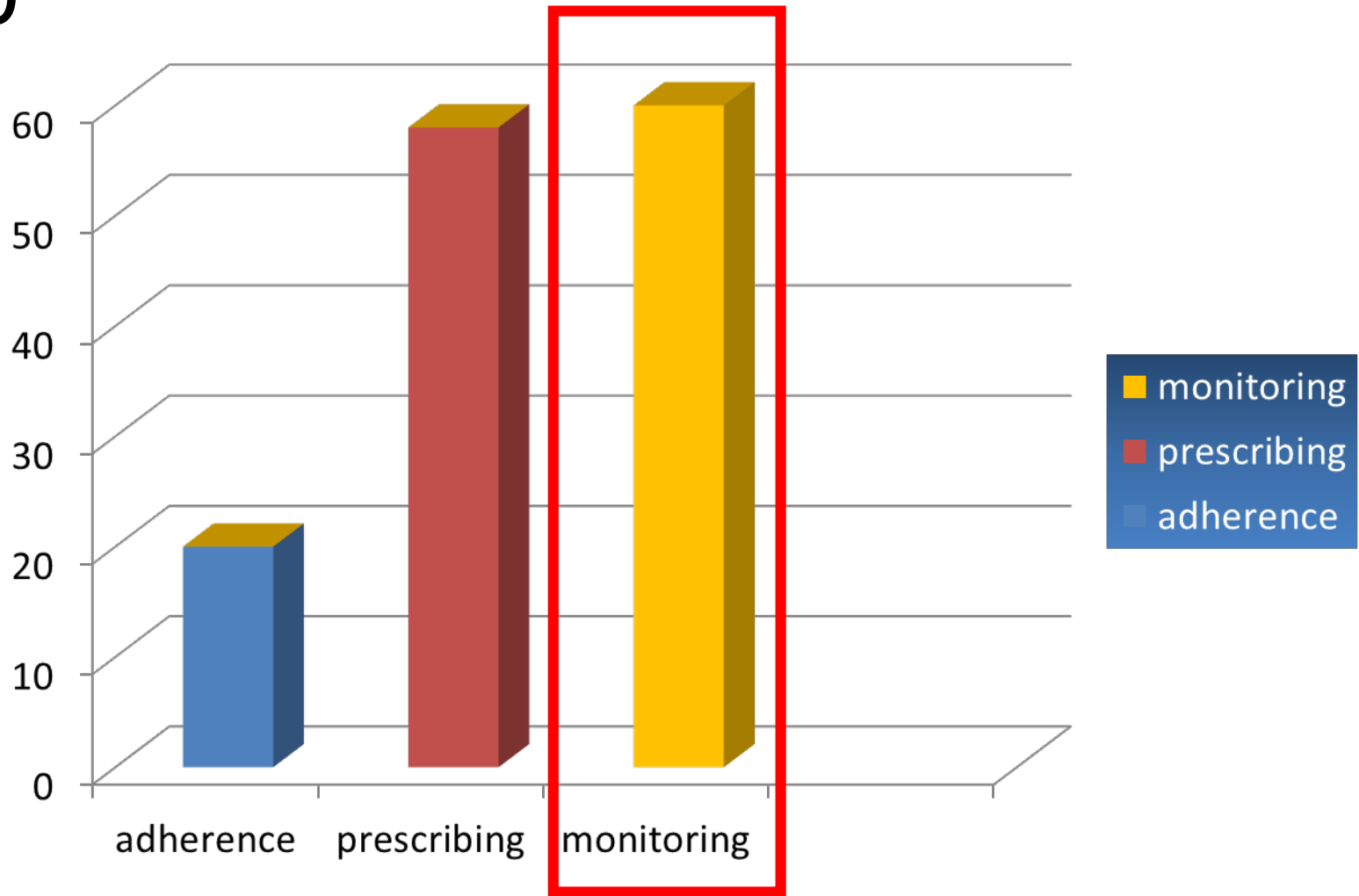
Adherence:

- HC system obsessed
- Strongest driver = the belief that the product works for a problem the patient is concerned about.
- Cochran review concludes despite multiple complex interventions, none have yet to successfully improve adherence.

Bokhour, B.G., 2006.

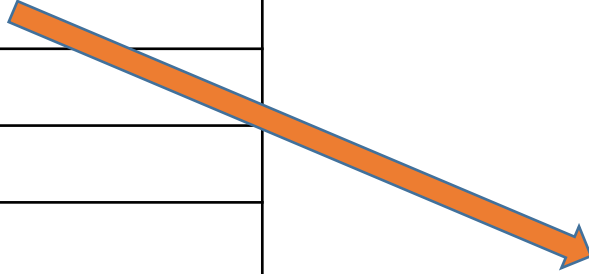
Kressin, N.R., 2007.

Clifford, S., 2008.



Gurwitz, JH., Field TS., Harrold LR., et al. Incidence and Preventability of Adverse Drug Events Among Older Persons in the Ambulatory Setting. JAMA March 5, 2003 Vol 2389, no 9 1107-1116

Year	# FDA approved drugs
2018	59
2017	46
2016	22
2015	45
2014	44
2013	27
2012	43



[FDA New Molecular Entities 2016](#)

[FDA Approved Drugs 2016](#)



- PDR in 1969 = 1425 pages Rx and OTC

- PDR in 2012 = 3151 very different pages plus a separate 800-page OTC product book.

85 drugs pulled off market since..... ever.

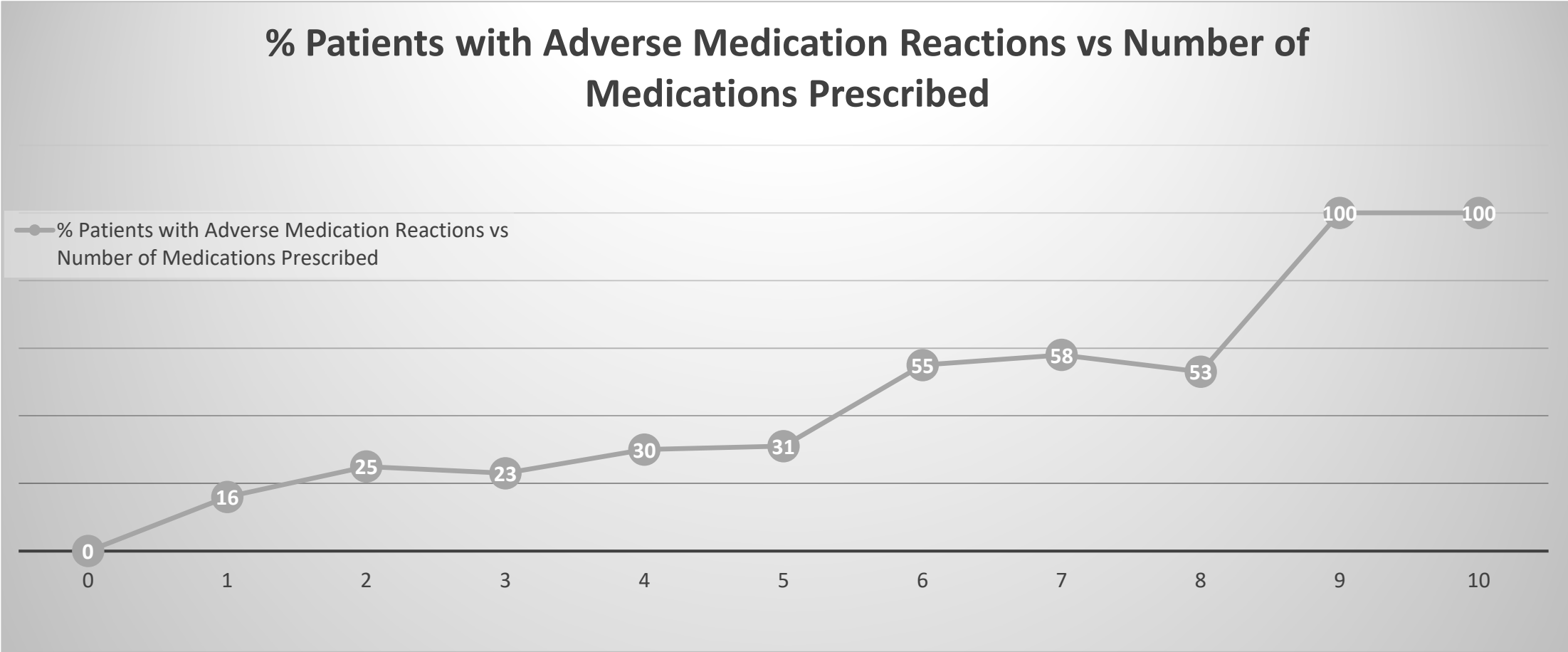
+ Over the Counter Products, Supplements and Vitamins



- U.S. Food & Drug Administration: <https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products>
- Center Watch: <https://www.centerwatch.com/drug-information/fda-approved-drugs/year/2016>
- US Government Publishing Office: https://www.ecfr.gov/cgi-bin/text-idx?SID=9f72be9edb31ecf7e76f977678b42878&mc=true&node=se21.4.216_124&rgn=div8



What's The Concern?

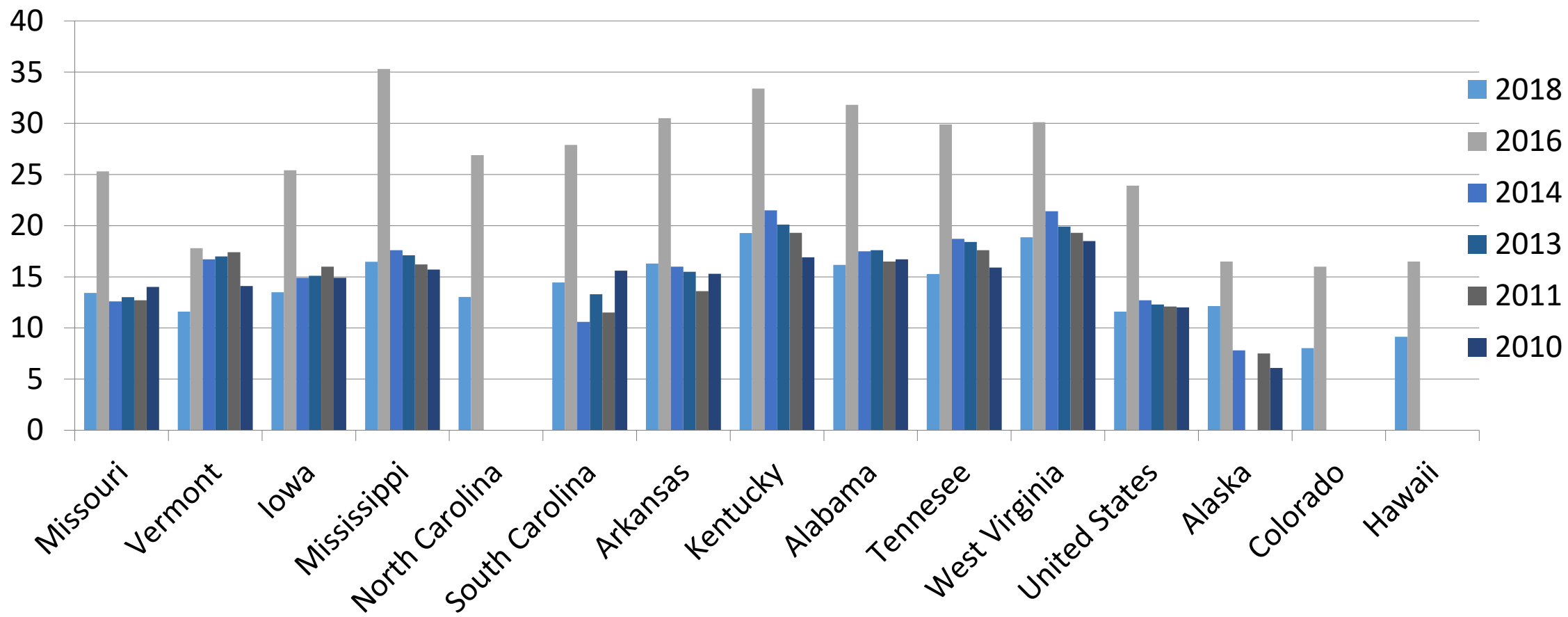


Is total drug burden important?

Intervention: Discontinuation of average 2.8 drugs per patient. 119 patient in geriatric nursing care in Israel vs age, gender and co-morbidity matched controls in the same facility.

	Study Group	Control Group
One-year mortality rate	21%	45%
Annual referral to ED	11.8%	30%
	Type of medication discontinued	Outcome
Example of meds discontinued	Nitrates in patients who had no chest pain for 3 months. Failure defined as return of symptoms or ECG changes.	22 patients had nitrates discontinued with no clinical or ECG changes.
	H2 blockers in patients with no proven peptic ulcer, gastrointestinal bleeding or dyspepsia for 1 year. Failure defined as return of UGI bleed.	Discontinuation of H2 blockers did not cause UGI symptoms in 94% of patients.
	When several antihypertensive agents were used, they tried to remove only one while maintaining the dosage of others. Failure defined as increase in dbp > 90mmHG or sbp>140 mmHG	Discontinuation of blood pressure medications did not cause increased bp in 82% (42/51) of patients.

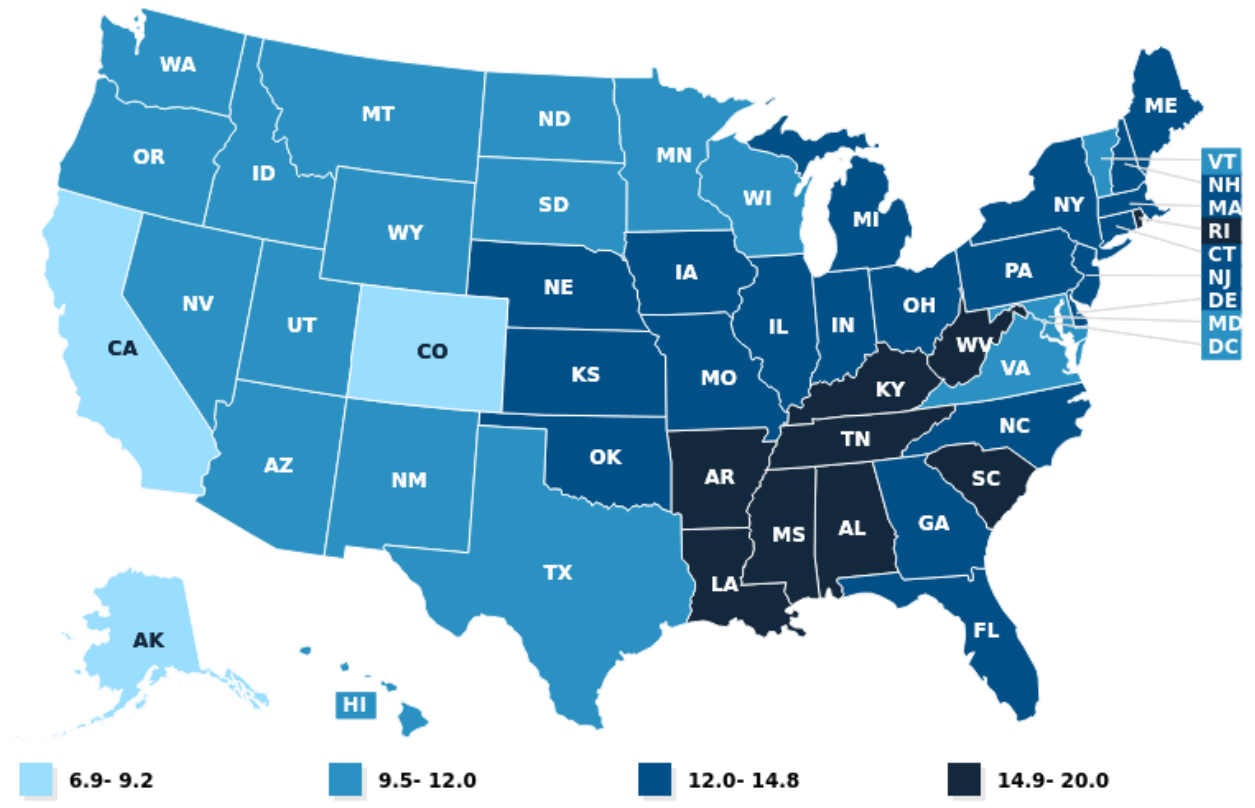
(Garfinkel, Zur-Gil et al. 2007)



1997 US Rx per Capita 8.9



Retail Prescription Drugs Filled at Pharmacies (Annual per Capita): Retail Rx Drugs per Capita, 2017



SOURCE: Kaiser Family Foundation's State Health Facts.

Is Polypharmacy a Harmful Syndrome for All?

>, or = to 20 years of age (median age 49)

- None, 1-3, 4-6, 7-9, 10 or >
- Not consistently linked with increased hospitalization among multi-morbidity patients.
- “Hyperpolypharmacy” associated with increased hospitalization risk across patient groups with any number of co-morbidities.

Payne, Abel et al. 2014

Middle Aged Adults (45-64 years)

- PROMPT Criteria for Middle Aged Adults
 - Example: Esomeprazole or Omeprazole should not be used in combination with clopidogrel.
 - Example: PPIs should not be prescribed at doses above the recommended maintenance dosage for > 8 weeks.
- Conflicting studies regarding the associations of polypharmacy in adults <60 years.

Appropriateness

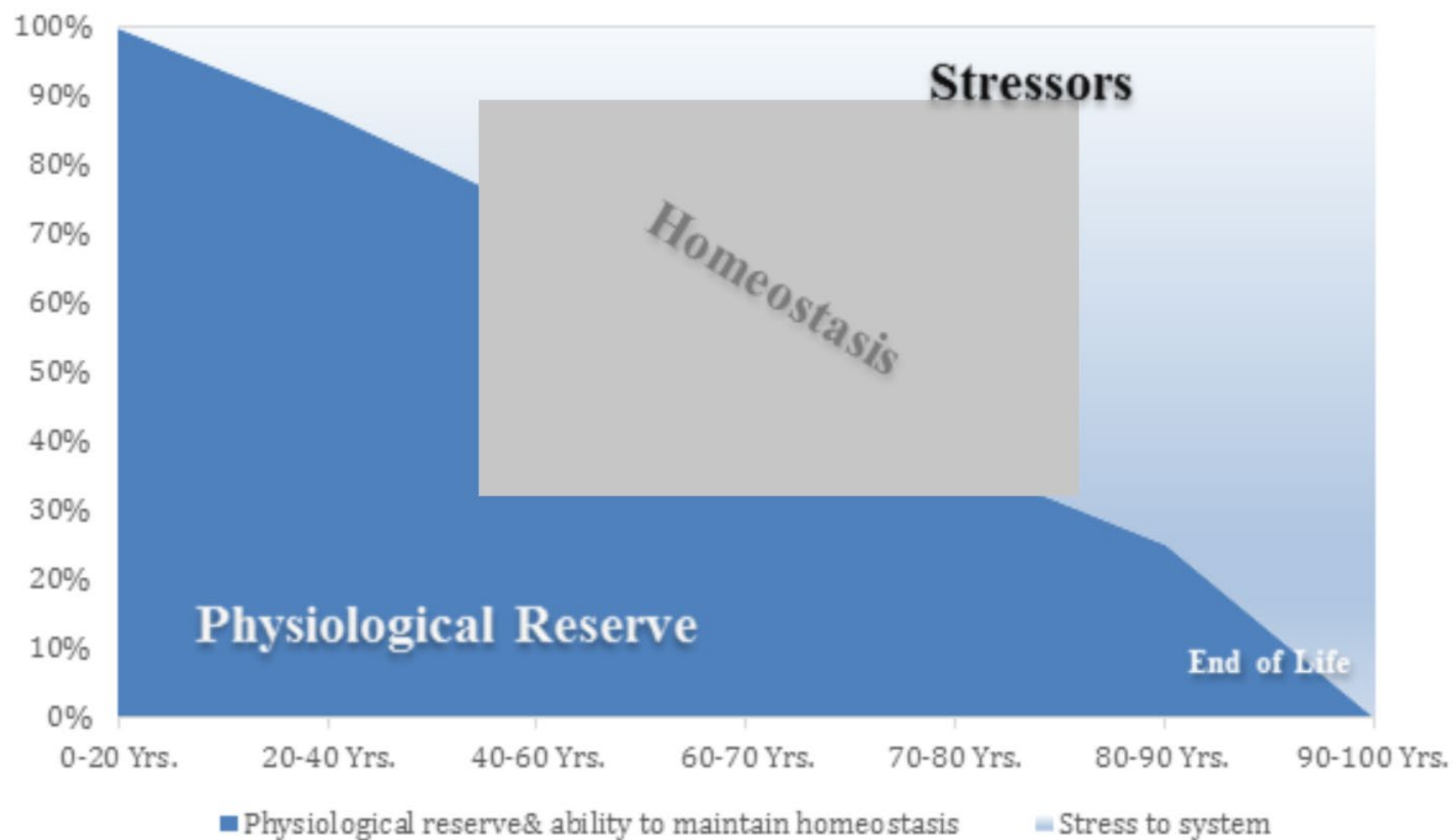
Cooper, Ryan et al. 2014
Calderon-Larranaga, Gimeno-Feliu et al. 2013

Older Adults

- > or = to 5 medications
- Poor outcomes; frailty, disability, mortality, and falls.

Nobili, Licata et al. 2011
Franchi, Marcucci et al. 2016
Gnjidic, Hilmer et al. 2013; Steinman, Miao et al. 2014

Ability to Tolerate Stressors to System Over Time



How do stake holders
view medication
use?



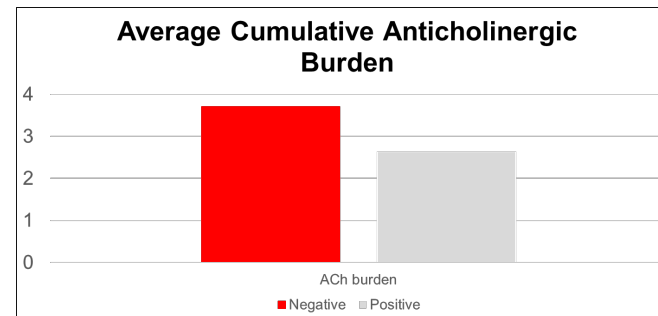
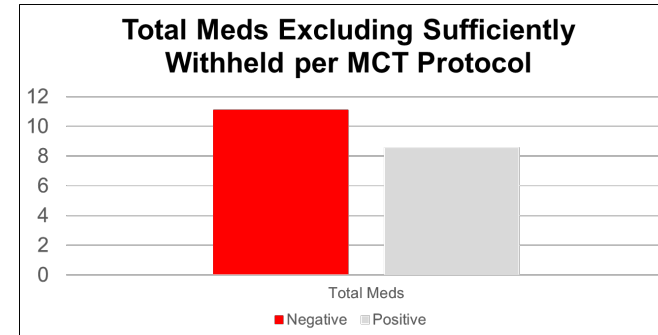
**"If you remember, I did mention possible
side-effects."**



Efficacy is great but what about toxicity? Pharmacology and Toxicology go hand in hand...or they're supposed to at least.

Perhaps a Shift in Approach to Research is Needed Too

Medications	ATS Hold Protocol	UL hold Protocol	T _{1/2} (expected elimination for adults)	T _{1/2} (expected elimination for older adults)
Salmeterol	48 hrs	48 hrs (Advair 24 hrs)	5.5 hrs (27.5 hrs)	Increased T _{1/2} with high drug burden of CYP3A4 metabolized medications.
Formoterol	48 hrs	48 hrs (Symbicort 24 hrs)	7-10 hrs (35-50 hrs)	60+: 11 hrs (55 hrs) 80+: 12 hrs (60 hrs) 90+: 13 hrs (65 hrs)
Ipratropium	48 hrs	48 hrs	2 hrs (10 hrs)	2 hrs (10 hrs)
Tiotropium	48 hrs	48 hrs	Solution [Asthma]: 44 hrs(220 hrs)	Solution[asthma]: 60+: 48.4 hrs (242 hrs) 70+: 52.8 hrs (264 hrs) 80+: 57.2 hrs (286 hrs)
Theophylline	12-24 hrs	12-48 hrs	8.7 hrs (43.5 hrs)	9.8 hrs (49 hrs)
Cetirizine	12-14 hrs	72 hrs	8 hrs (40 hrs)	T _{1/2} will increase with renal impairment



William Osler

“The desire to take medicine is perhaps the greatest feature which distinguishes man from animals.”





Thank You.

What's up in your world regarding Polypharmacy?