What have we learned from 40 years of research on medication adherence?

The 40,000 foot view of nearly 40,000 articles

Mitch DeKoven, MHSA
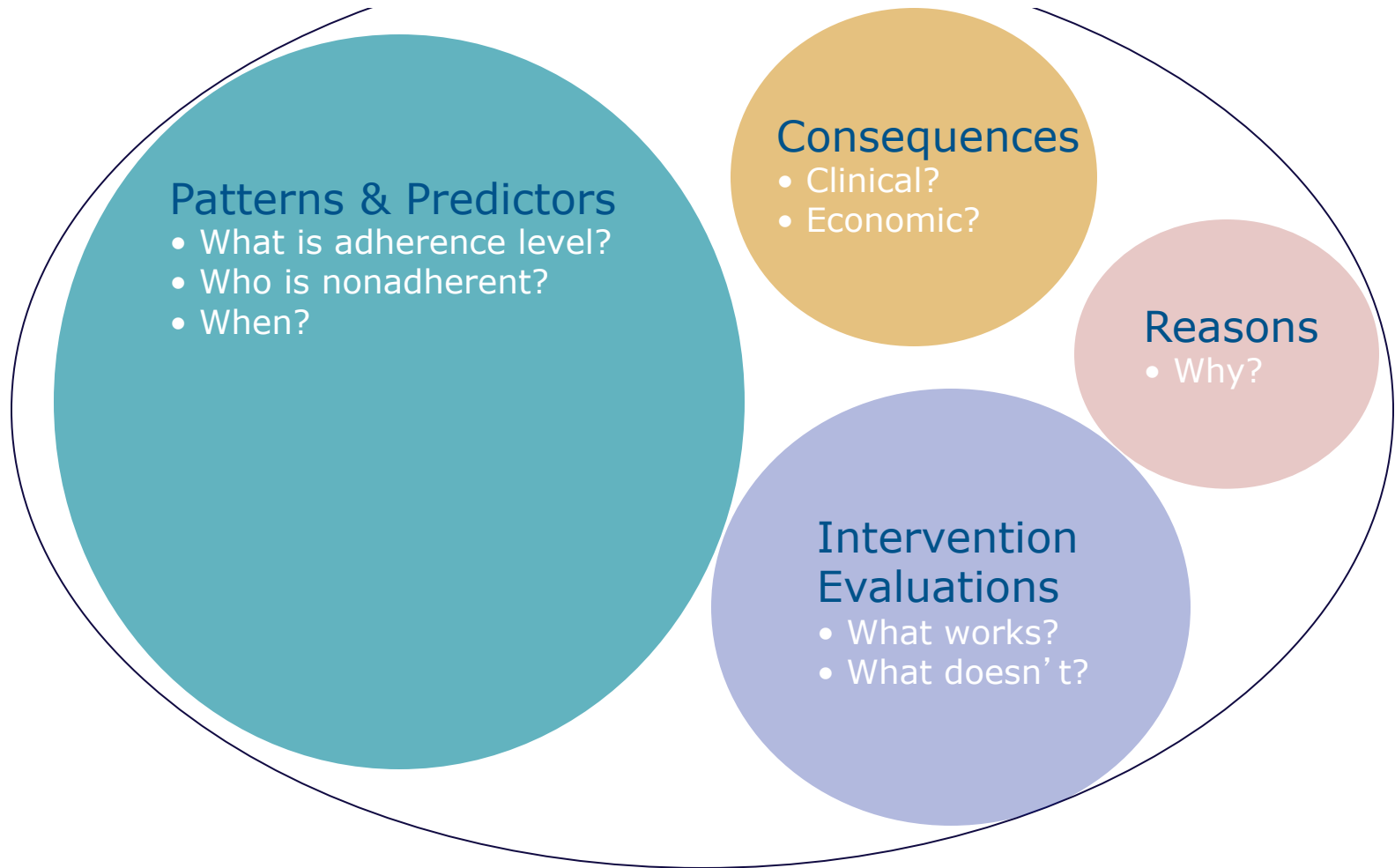
It's a jungle out there:
What have we learned from 40 years of adherence research?

The existing literature can be organized into 4 large categories based on specific aims

Patient Compliance/Adherence Literature

Patterns & Predictors
- What is adherence level?
- Who is nonadherent?
- When?

Consequences
- Clinical?
- Economic?

Reasons
- Why?

Intervention Evaluations
- What works?
- What doesn't?

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"Patterns and predictors" studies define the problem and highlight nonadherence as a public health issue

Patterns & Predictors
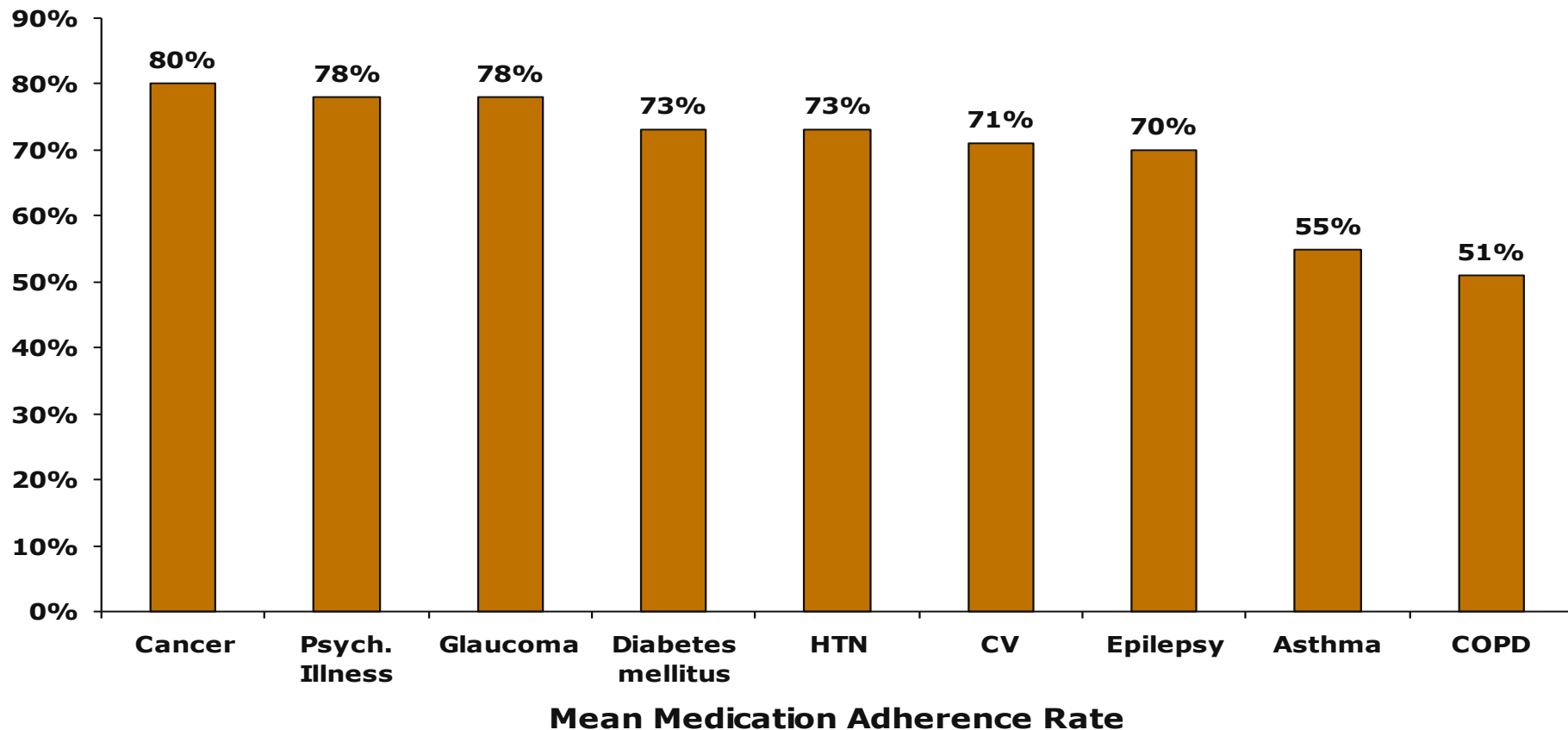- What is adherence level?
- Who is nonadherent?
- When?

- This is the largest subgroup of papers in the literature

- Describes adherence or persistence in the therapy area of interest

- Can be used to segment the population by adherence level on a number of characteristics

Urquhart's framework is useful because it identifies discrete phases of prescription drug utilization
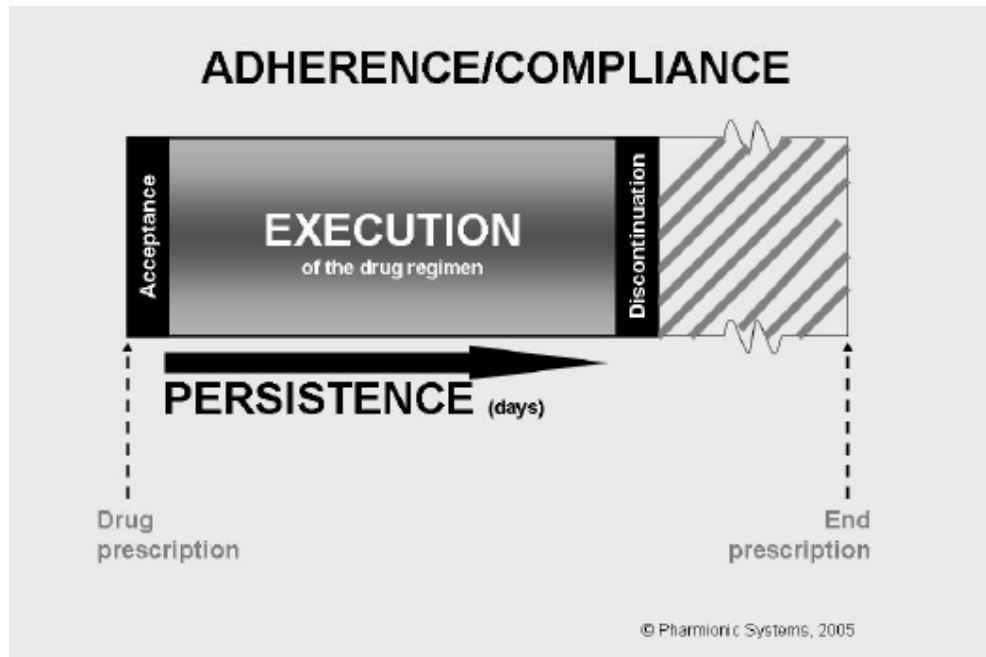
- Analyze and address quality of execution and persistence separately

- Recognize that quality of execution influences persistence

Urquhart, *The European Journal of Hospital Pharmacy Science*, 2005

Claxton's systematic review compared medication "execution" rates* across therapy areas

Bar chart: Mean Medication Adherence Rate

Therapy Area	Rate
Cancer	80%
Psych. Illness	78%
Glaucoma	78%
Diabetes mellitus	73%
HTN	73%
CV	71%
Epilepsy	70%
Asthma	55%
COPD	51%

Mean Medication Adherence Rate

* Does not encompass persistence, accounting for relatively high rates shown.

Claxton, *Clin Ther*, 2001

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"Predictors" are measurable characteristics associated with nonadherence

The following categories of predictors have been studied:

- Patient characteristics
  - Demographic
  - Clinical
  - Health services use
  - Prior medication adherence

- Provider characteristics/ relationship
  - Specialty
  - Patient assessment of relationship

- Regimen characteristics
  - Out of pocket cost
  - Effectiveness
  - Tolerability
  - Frequency
  - Route of administration
  - Complexity

- Health system characteristics
  - Type of health insurance
  - Pharmacy benefit design

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Predictors can be prioritized based upon the reliability of their association with adherence

Variables	Utility as a Predictor	Explanation
• Patient demographics (age, sex, race, SES)	Weak	Literature lacks consensus Usefulness depends on therapeutic area and patient population
• Relationship between patient and providers • Regimen characteristics • Patient clinical status • Patient health services use • Health system characteristics	Moderate	General consensus in literature Effect may vary by therapeutic area and population
• Time since initiation • Past adherence	Strong	Always the strongest predictors and easy to measure

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The clinical and economic burden of nonadherence is well-established, but with methodological caveats

Consequences
- Clinical
- Economic

- This is a rapidly growing subgroup of papers in the literature

- Describes cascade of clinical and economic outcomes in patients who are nonadherent

- Precision is difficult due to methodological limitations inherent in observational studies

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The overall cost of nonadherence to the health care system is staggering

- 125,000 deaths per year in U.S.[1]

- Total cost estimates range from $100 billion[2] to $300 billion[3], including both direct and indirect costs.

Therapy areas in which the burden of nonadherence is especially well documented are:

- Hypertension
- Diabetes
- HIV/AIDS
- Depression
- Schizophrenia
- Dyslipidemia
- Tuberculosis
- Immunosuppressive therapy
- Oncology

[1] Cited by Haynes RB. *Compliance in Healthcare*, 1979; Blackwell B. *N Engl J Med*, 1973.
[2] Cited by Munger, Liu, Wertheimer, Whitcup, Berg, Ickovics, Burney, Biondi-zoccai
[3] DiMatteo, *Med Care*, 2004.

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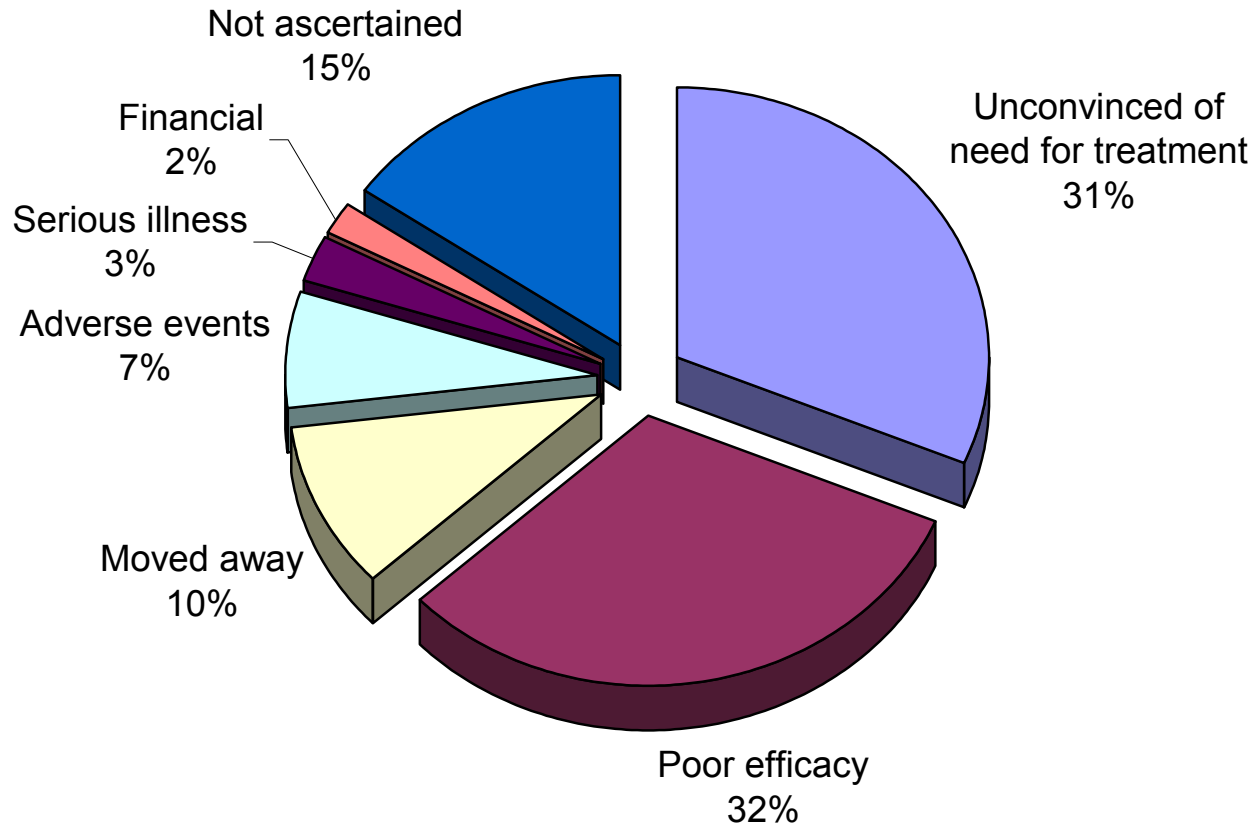# Patient-reported reasons for nonadherence are a critical input into the development of interventions

Reasons
- Why?

- This is a small subgroup of papers in the literature

- Requires survey work with patients, which is time consuming and costly

- Requires psychological expertise to avoid response biases

- Essential element in program development

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Often, the best available data on reasons for nonadherence are dated or from other countries

Not ascertained
15%

Financial
2%

Serious illness
3%

Adverse events
7%

Moved away
10%

Unconvinced of
need for treatment
31%

Poor efficacy
32%

Simons, et al. *Med J Austr* 1996

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Some general reasons for nonadherence apply to multiple therapy areas

- Unconvinced of need for therapy
  - Never needed it
  - Need went away (cured)
  - Competing health priorities
- Unconvinced of effectiveness
- Experienced/feared side effect
- Difficulty with administration
  - Routine
  - Route (needles, inhaler)
- Out of pocket cost
  - Of subject medication
  - Of other medications
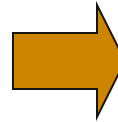
Relative importance and specifics vary by therapy area (and even by drug)

These barriers should be directly addressed in interventions

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Rigorous program evaluations are key to knowing best practices for improving adherence

Intervention Evaluations
- What works?
- What doesn't?

- This is a large subgroup of papers in the literature

- Quality has been described as "generally poor" which casts doubt on conclusions (both positive and negative)

- But several comprehensive review papers provide insight and promising directions

- Literature on health system factors (e.g., changes in benefit design) is emerging

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Anatomy of an adherence intervention synthesis: What works in hypertension and cholesterol

The authors reviewed 62 studies describing 79 compliance interventions for antihypertensive and lipid lowering medications

- 56% were reported to improve compliance
- 12 interventions could be recommended based on minimum methodological standards
  - Control group
  - Objective measurement of compliance
  - At least 6 months of follow-up
  - Statistically significant improvements in compliance

Recommended Interventions:*

1. Fixed dose combination therapy
2. Reducing frequency to QD or QW
3. Unit dose packaging
4. Computerized telephone counseling
5. Weekly calls from pharmacist (12)
6. In-pharmacy disease management visits
7. Pharmacist + nurse + dietician disease management clinic
8. Mailed reminders
9. Reminders + unit dose packaging
10. Appt reminders + home visits + diaries
11. Schedule tailoring + self-monitoring + diaries + rewards
12. Educational materials + phone counseling + newsletters + refill reminders

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Meta-analyses across therapy areas suggest specific intervention attributes that are effective

To be successful, a program must:

1. Be delivered by a trusted source
2. Be 'personalized' to the patient's situation
3. Reinforce medical need and expected outcomes
4. Segment and target at-risk populations
5. Reinforce/reward initiation and maintenance

Effective interventions combine education, motivation, support, reminders and rewards

Haynes et al. *Lancet* 1996;348:383-6
Newell SA, et al. *Prev Med* 1999;29:535-548
Roter D, et al. *Med Care* 1998;36:1138-1161
McDonald HP, et al. *JAMA* 2002;288:2868-2879

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Conclusions and recommendations:
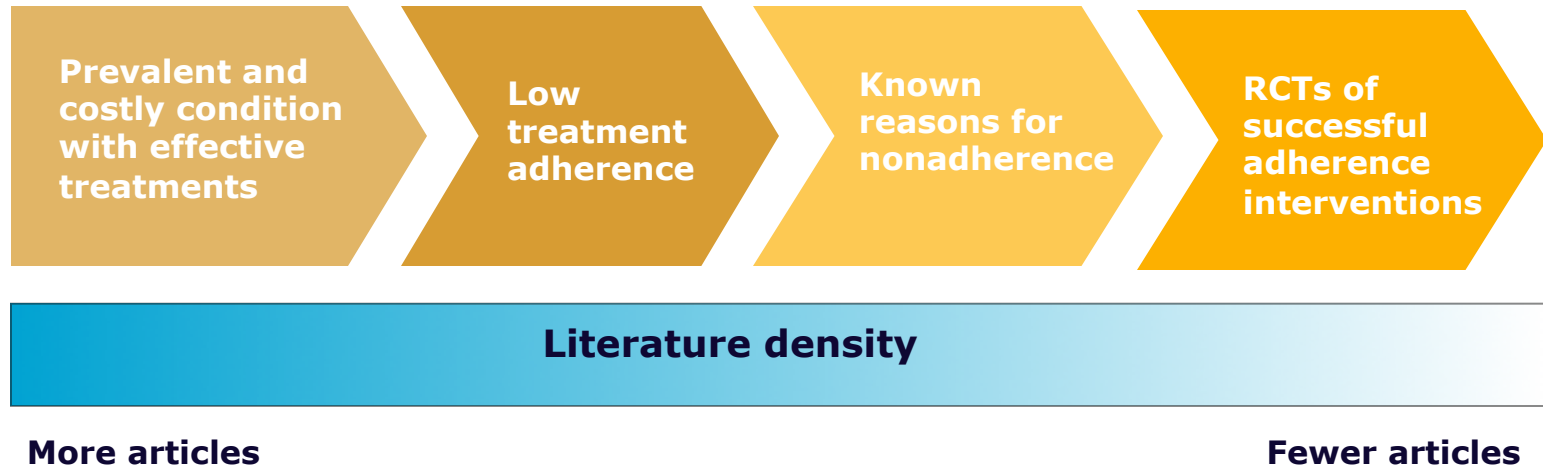What do we know from the literature and where do we go from here?

As we think about designing a national campaign, it is important to note some remaining unanswered questions

- How should adherence be measured?
  - Lack of consensus on target level of adherence
  - Different methods are used
  - Follow-up time varies across studies
  - Best practices may be an issue/question

- What interventions will be most effective, and cost-effective, at the population level?
  - Do they include psychological components?

- How will new and upcoming quality performance measures affect levels of adherence?
  - Other policy changes to achieve greater engagement by stakeholders?

There is no silver bullet as components of interventions will vary by disease state, readiness to change, time on therapy, etc.

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The opportunity to improve adherence is greatest in therapy areas where the research meets 4 criteria

Prevalent and costly condition with effective treatments → **Low treatment adherence** → **Known reasons for nonadherence** → **RCTs of successful adherence interventions**

Literature density

More articles   **Fewer articles**

Relatively few therapy areas meet all of these criteria:

- Hypertension
- Dyslipidemia
- Asthma
- Diabetes
- HIV/AIDS
- Depression
- CHF
- Osteoporosis

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