Pharmacoepidemiology in action: adherence to medicines regimes

Kathleen Bennett, Department of Pharmacology & Therapeutics
Trinity Centre for Health Sciences, St James's Hospital, Dublin

TRINITY COLLEGE DUBLIN

NHS
National Institute for
Health and Clinical Excellence

Medicines adherence

Involving patients in decisions about prescribed medicines and supporting adherence

Issued: January 2009

NICE clinical guideline 76
guidance.nice.org.uk/cg76

Poor Adherence to Medicines

* Poor medication adherence is the primary reason for suboptimal clinical benefit of therapy. [1]

* WHO REPORT, NIHR:
* Estimated that 30-50% medicines for long term conditions not taken as directed.[1]
* Effective interventions are elusive. [2,3]

[1] WHO report on adherence 2003. 2. Haynes et al Lancet 1996 3. Haynes et al Cochrane 2002

Why adherence matters

"Of all medication-related hospital admissions in the United States, 33 to 69 percent are due to poor medication adherence, with a resultant cost of approximately $100 billion a year."

Results of failure to adhere to prescribed medications:

- Increased hospitalization
- Poor health outcomes
- Increased costs
- Decreased quality of life
- Patient death

Benner JS, Glynn RJ, Mogun H, Neumann PJ, Weinstein MC, Avorn J. Long-term persistence in use of statin therapy in elderly patients. JAMA 2002;288:455-461

Example: type 2 diabetes

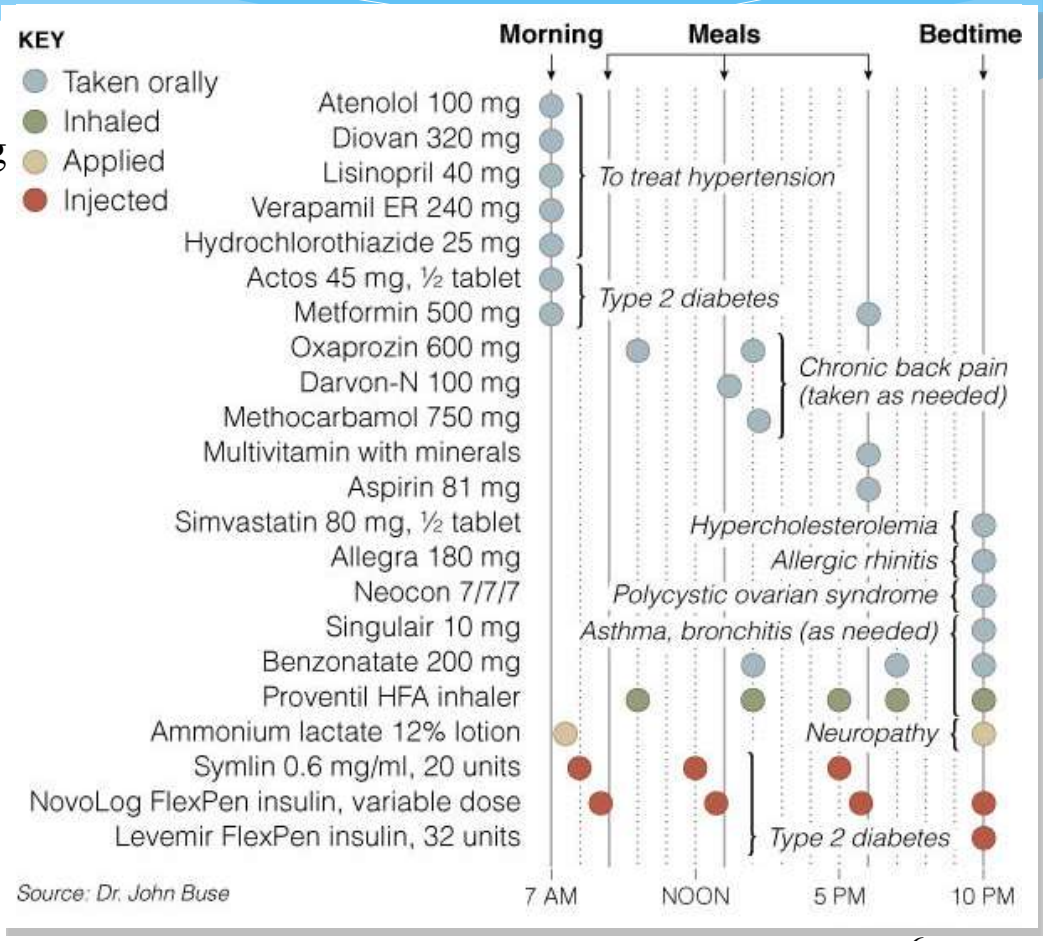
* Progressive disease
* Multi-system disease with co-morbidities—polypharmacy!
* Complex guidelines
* Unmet needs of pharmacotherapy
* In order to reduce diabetes-related complications, blood pressure and blood lipids control as well as foot care are necessary. All this requires a substantial degree of treatment adherence from patients.

The treatment complexity in type 2 diabetes drives non-adherence to management strategies

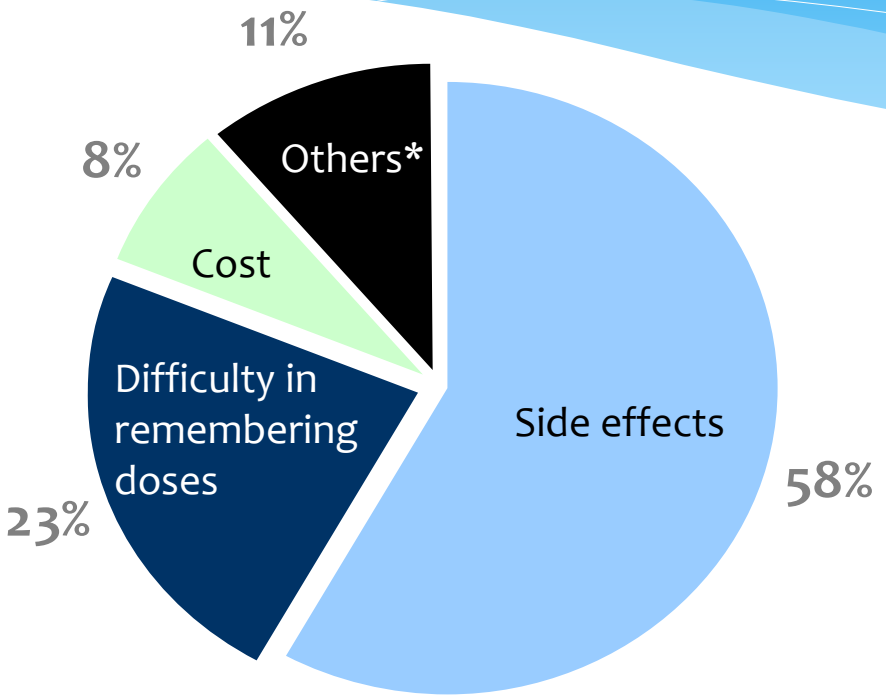
Medication for Complex Diabetes

A 42-year-old woman's regimen for treating complex diabetes includes…

- At least 15 types of oral medication
- 2 over-the-counter products
- 7 to 10 injections
- 4 blood tests



Most common factors related to non-adherence in patients with type 2 diabetes



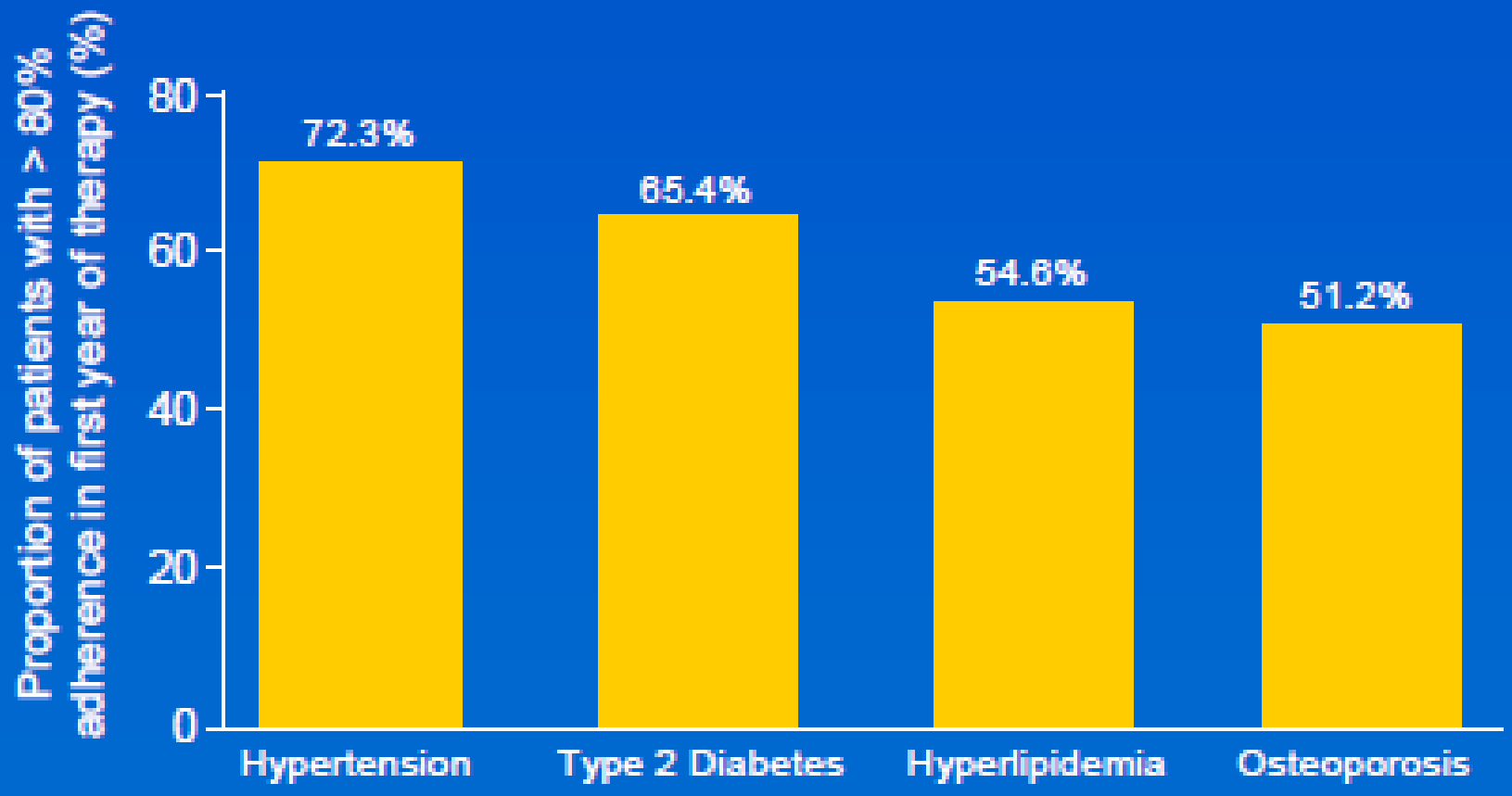
Only 23% of patients who had side effects reported the problems to their primary care physician

*Number of prescribed medications, patient characteristics

N=128 patients with Type 2 Diabetes.

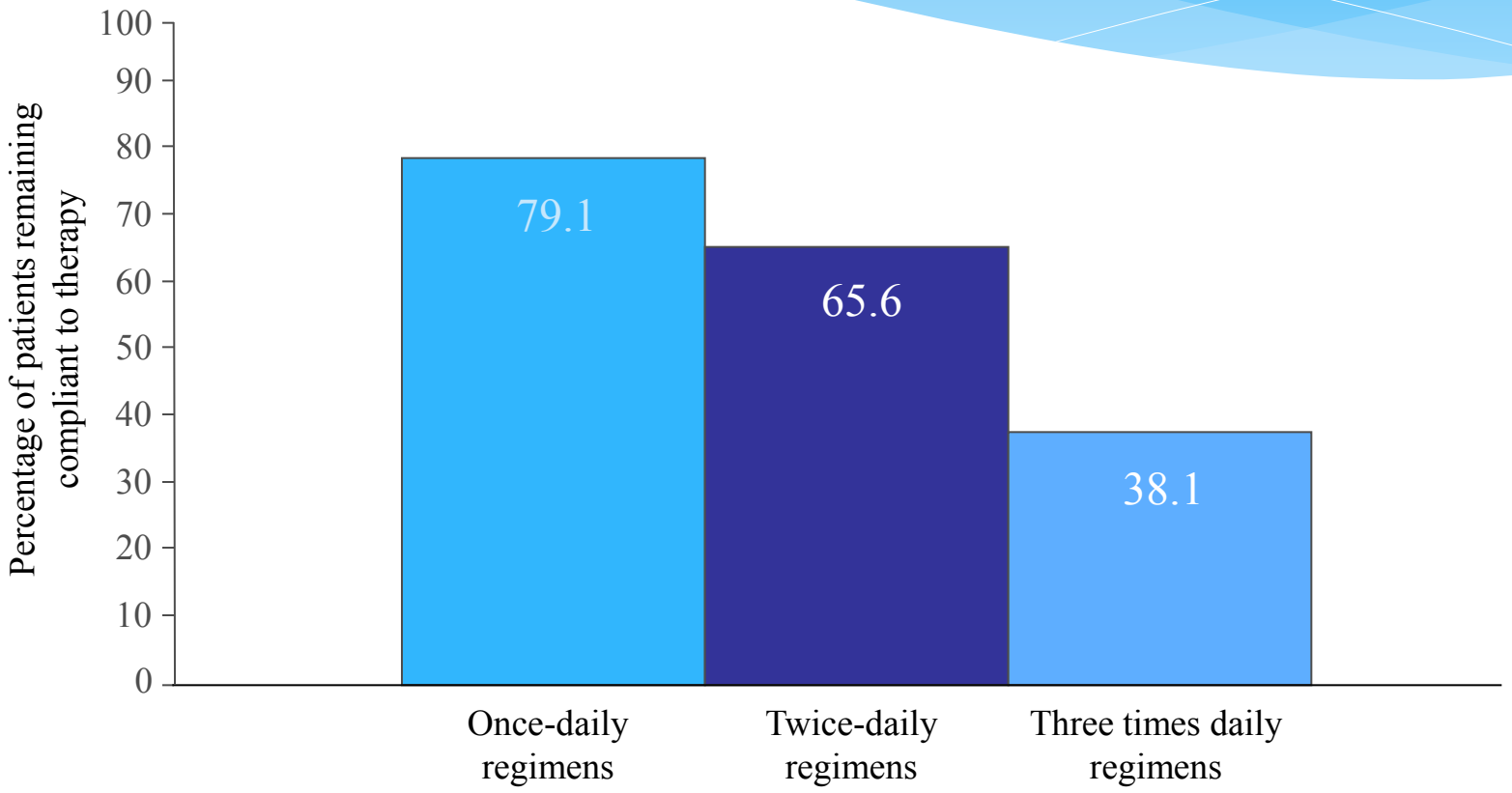
Grant RW et al. *Diabetes Care*. 2003;26:1408-1412.

Poor Adherence is Common in Chronic Conditions



Lekkerkerker F, et al. *Osteoporos Int* 2007.
Briesacher BA, et al. *Pharmacotherapy* 2008.

Adherence to oral anti-diabetes agents



Cramer J. *Diabetes Care*. 2004;27:1218-1224.

Myths of poor adherence

Feature of the disease

* Not linked to disease
* Low adherence problematic across most chronic disease
  * HIV[1]
  * Cancer[2]
  * Heart disease[3]

Non-compliant/deviant patient

* No clear consistent link between adherence and age, gender, marital status, education, etc
* Inconsistent, e.g. older age associated with non-adherence in some studies and not in others

1 Friedland, AIDS 1999; 2 Lilleyman, BMJ 1996; 3 Horwitz Lancet 1990

Myths of poor adherence

Simplifying the regime/reducing bill burden

* Can be helpful for some patients but not all
* Complexity not necessarily the issue but how the treatment regime fits with patients routine, expectations, preferences.

Providing clear instructions/information is enough

* Not always understood why medicines need to be taken.
* Concerns aboutthe side effect profiles.

HSE-PCRS pharmacy claims data

* All medicines dispensed by pharmacists under the
  * General Medical Services
  * Drug Payment Scheme
  * Long term illness
* Eligibility for GMS means tested <70 years, all eligible 70+ from 2001-Dec 2008.
* Drugs coded to WHO ATC classification
* Dose and duration available in addition to all co-prescribed medicines, age group and gender.
* Allows research to be performed.

Early Discontinuation of Tamoxifen

A Lesson for Oncologists

Thomas I. Barron, MSc[1]
Róisín M. Connolly, MB[2]
Kathleen Bennett, PhD[1]
John Feely, MD[1]
M. John Kennedy, MB[2]

[1] Department of Pharmacology and Therapeutics, Trinity College Dublin, Trinity Centre for Health Sciences, St. James's Hospital, Dublin, Ireland.

[2] Academic Unit of Clinical & Molecular Oncology, Trinity College Dublin & St James's Hospital, St. James's Hospital, Dublin, Ireland.

BACKGROUND.
fen therapy f
tions of adju
outcomes for
of tamoxifen
older using p
METHODS. A
therapy was
tamoxifen pe
between non
RESULTS. Wit
persistence r

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY (2013)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3535

ORIGINAL REPORT

An observational study examining the effect of comorbidity on the rates of persistence and adherence to newly initiated oral anti-hyperglycaemic agents

Miriam P. O'Shea*, Mary Teeling and Kathleen Bennett

ELSEVIER

journal homepage: www.elsevier.com/locate/jval

The Clinical and Economic Burden of Poor Adherence and Persistence with Osteoporosis Medications in Ireland

Mickaël Hiligsmann, PhD[1,2,3,], Bernie McGowan, MSc[3], Kathleen Bennett, PhD[4], Michael Barry, PhD[5], Jean-Yves Reginster, MD, PhD[2]*

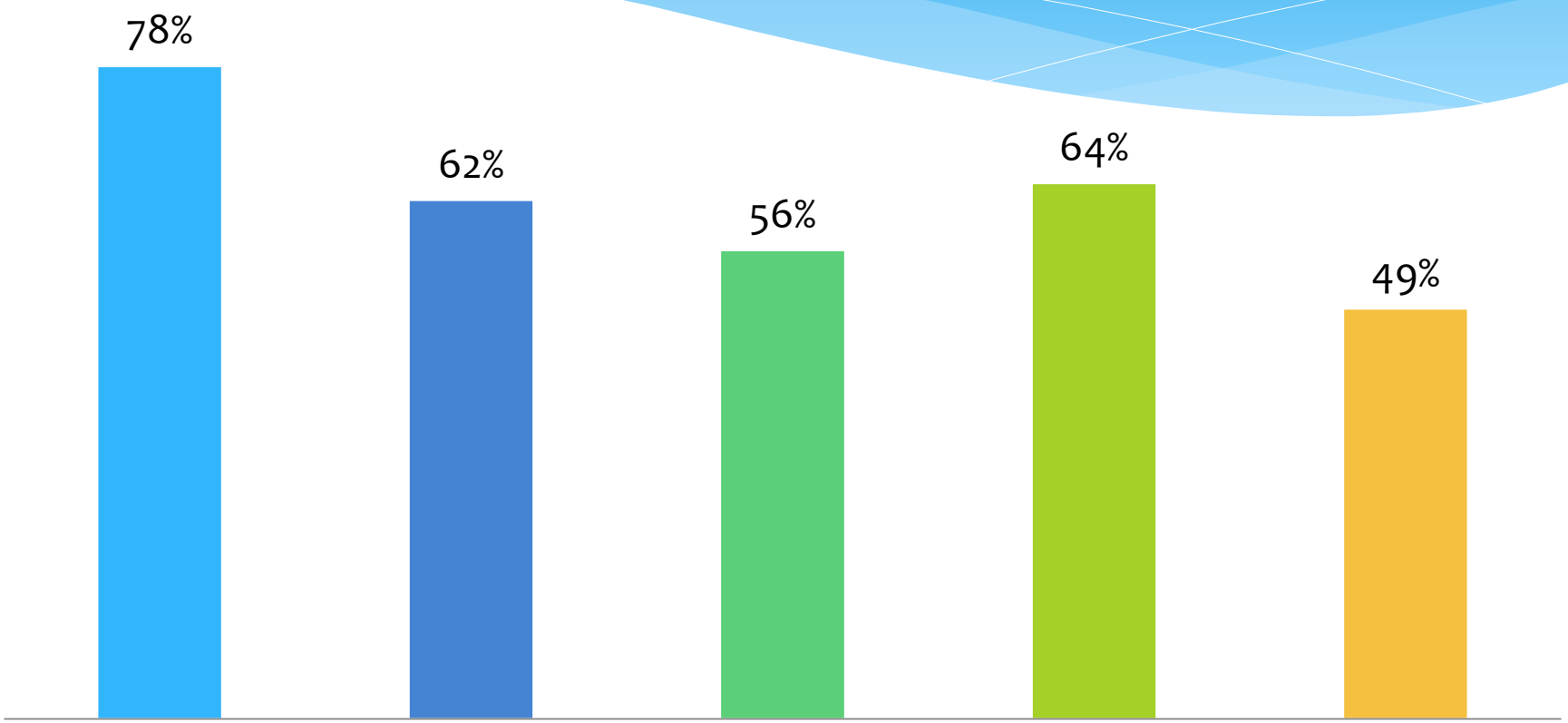
Eur J Clin Pharmacol (2013) 69:1467–1475
DOI 10.1007/s00228-013-1483-y

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

A population-based study of dosing and persistence with anti-dementia medications

Linda Brewer · Kathleen Bennett · Cora McGreevy · David Williams

Persistence at 1 year: Irish Health care system



Why is adherence important in diabetes?

* Diabetic patients do more than 95% of their own care
* Self management central to diabetes care.
  * Active monitoring
  * Adapting to changing conditions in diabetes treatment
  * Maintaining adequate metabolic control & Avoiding long term complications
* Adherence not just about medications but all self care.
* Poor adherence causes medical and psychosocial complications, reduces quality of life and wastes health care resources.
* Costs of treating type 2 diabetes was 4-6.5% of total healthcare expenditure in Ireland ; 50% hospitalisations due to complications [1]

Diabetes adherence in Ireland

* A cohort of 21,800 new OAH drug users was identified using the HSE-PCRS pharmacy claims database
* Persistence was 73.8% and 62.2% at 6 and 12 months respectively, similar to other reported studies

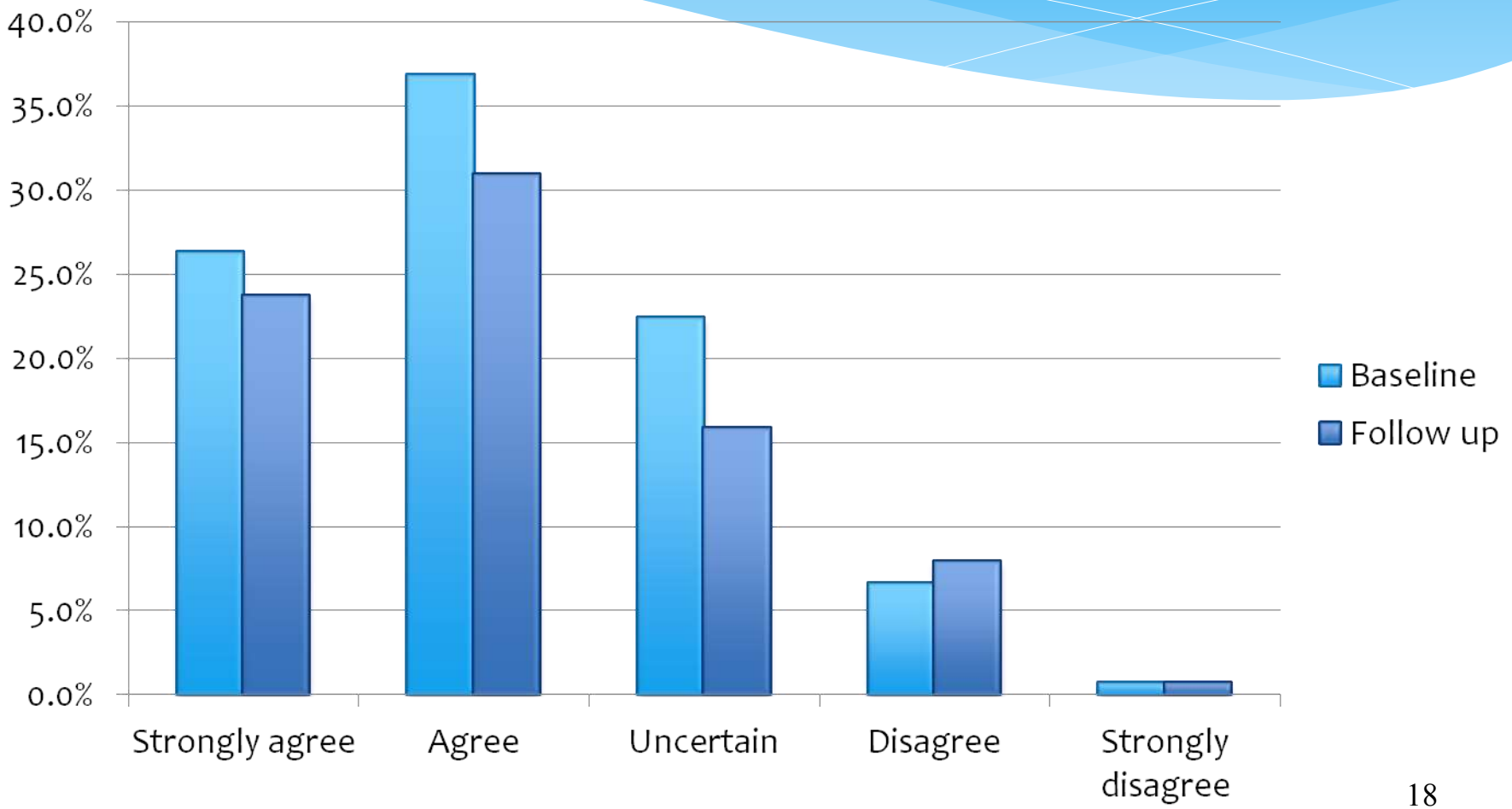
* Examined predictors of persistence; results for compliance similar

O'Shea, Teeling, Bennett, Pharmacoepidemiology & Drug Safety 2013

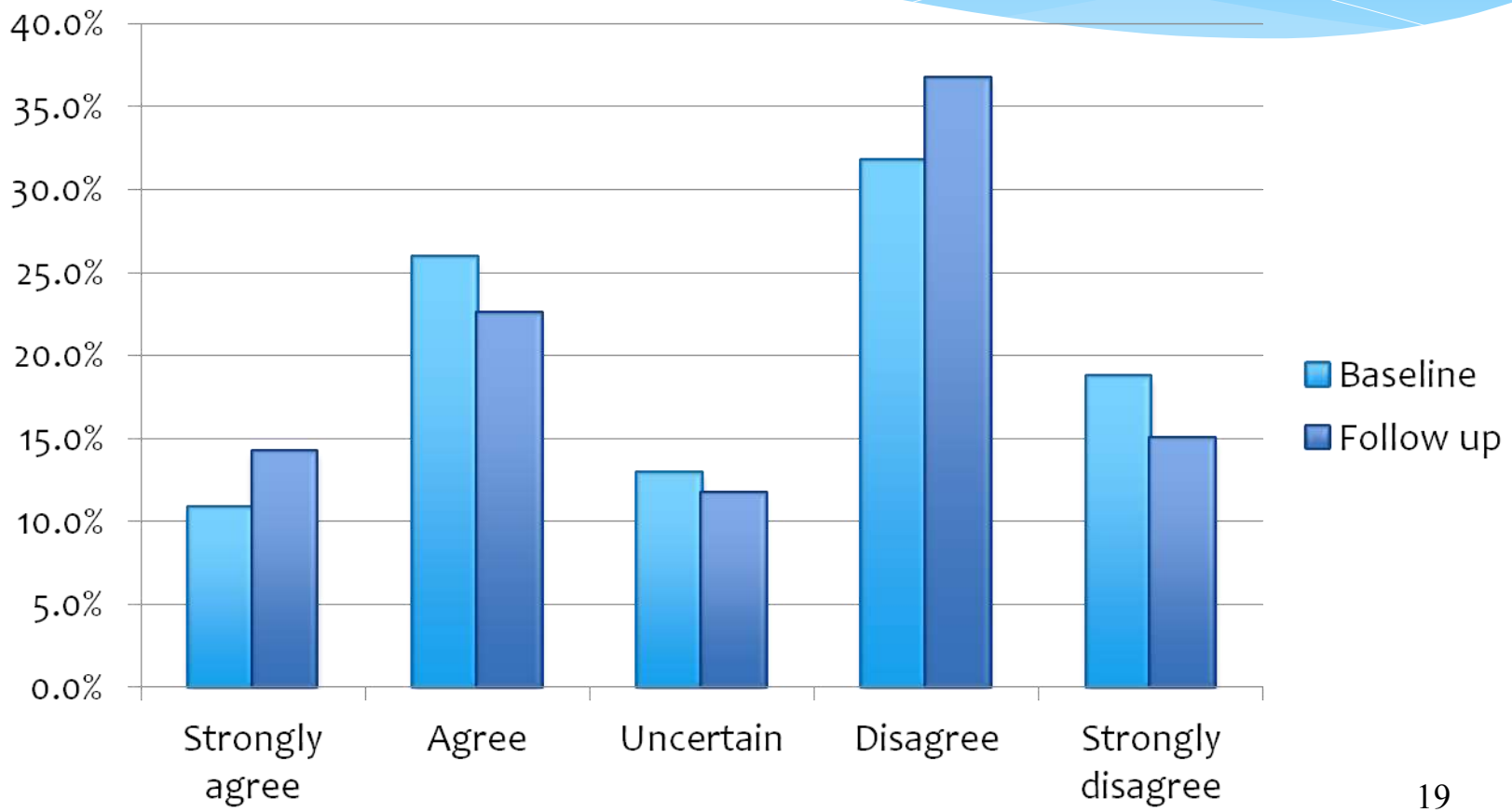
Predictors of persistence at 12 months

Variable	Adjusted OR	95%CI
Age (ref 25-34 yrs)		
35-44 years	1.71	1.39 - 2.12
45-54 years	1.86	1.52 - 2.28
55-64 years	2.07	1.70 - 2.58
65-69 years	2.09	1.69 - 2.58
70-74 years	1.88	1.53 - 2.31
>75years	1.22	1.00 - 1.49
Sex		
male vs. female	1.12	1.04 - 1.20
Comorbidity score		
7+ vs. None	7.5	6.50 - 8.67
OAH agent (ref metformin)		
sulphonylurea	0.66	0.60 - 0.72
metformin with a sulphonylurea	0.97	0.87 - 1.09
other combination	0.73	0.64 - 0.83

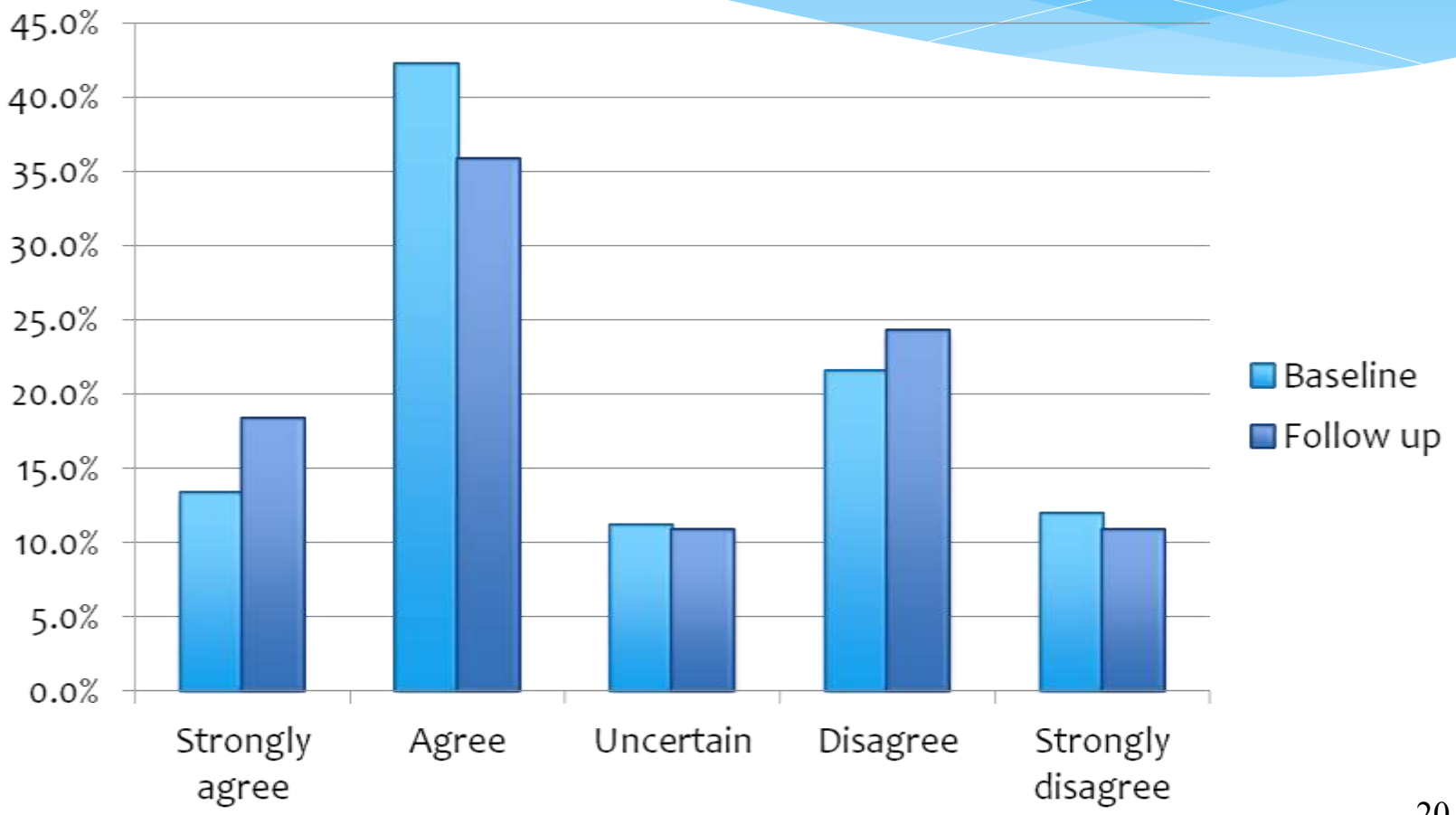
Beliefs in medicine: Without my medicines I would be very ill



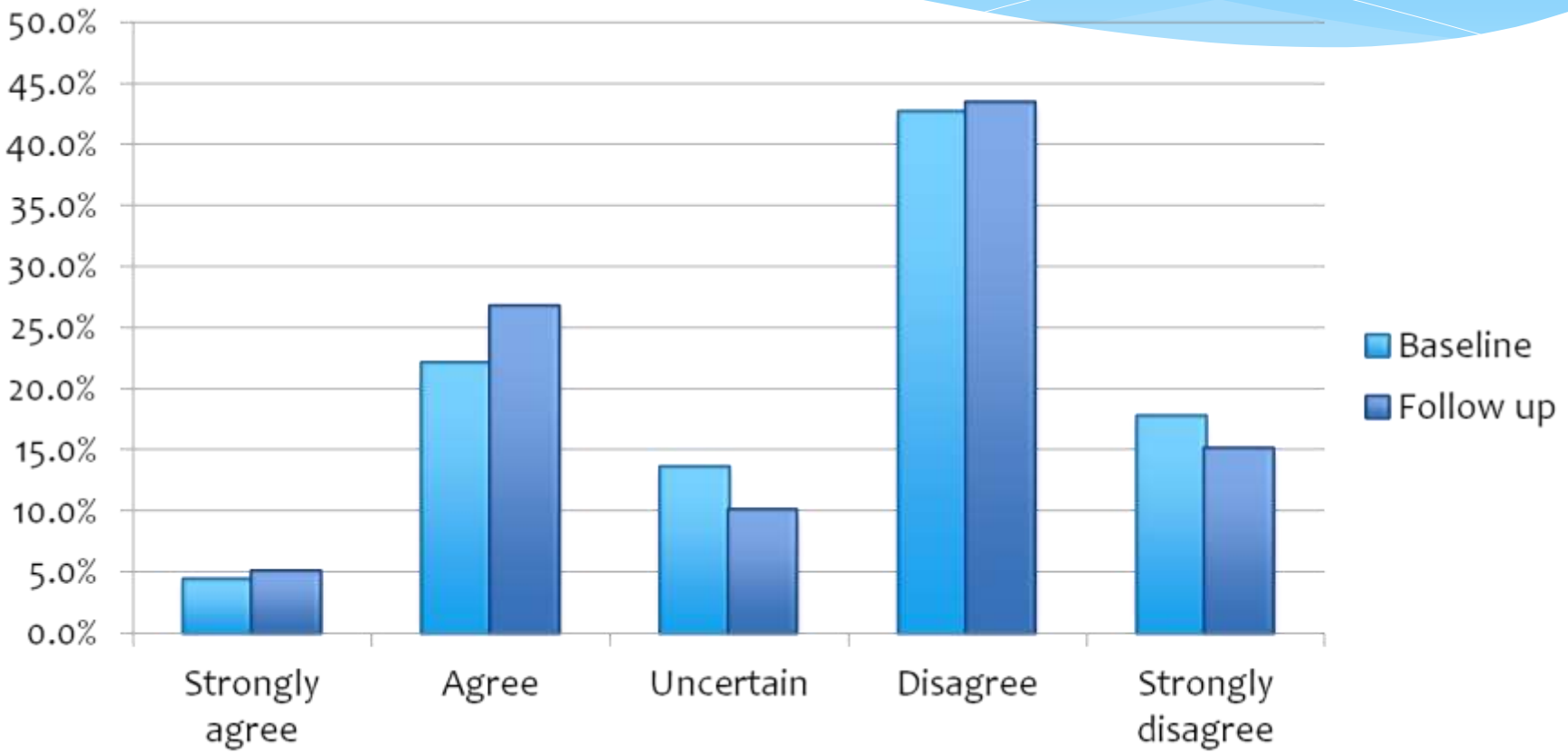
Having to take medicines worries me



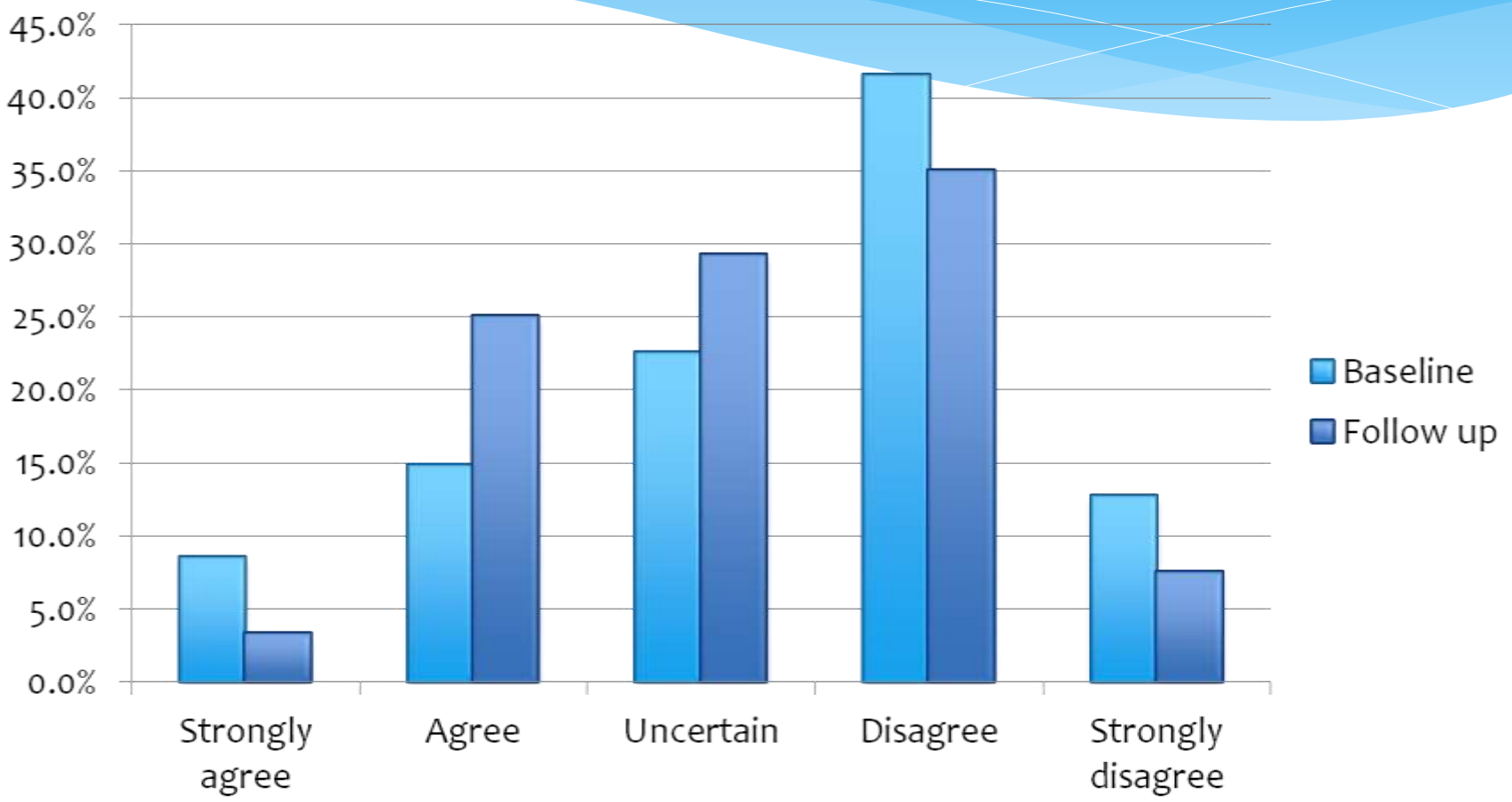
I sometimes worry about the long term effects of my medicine



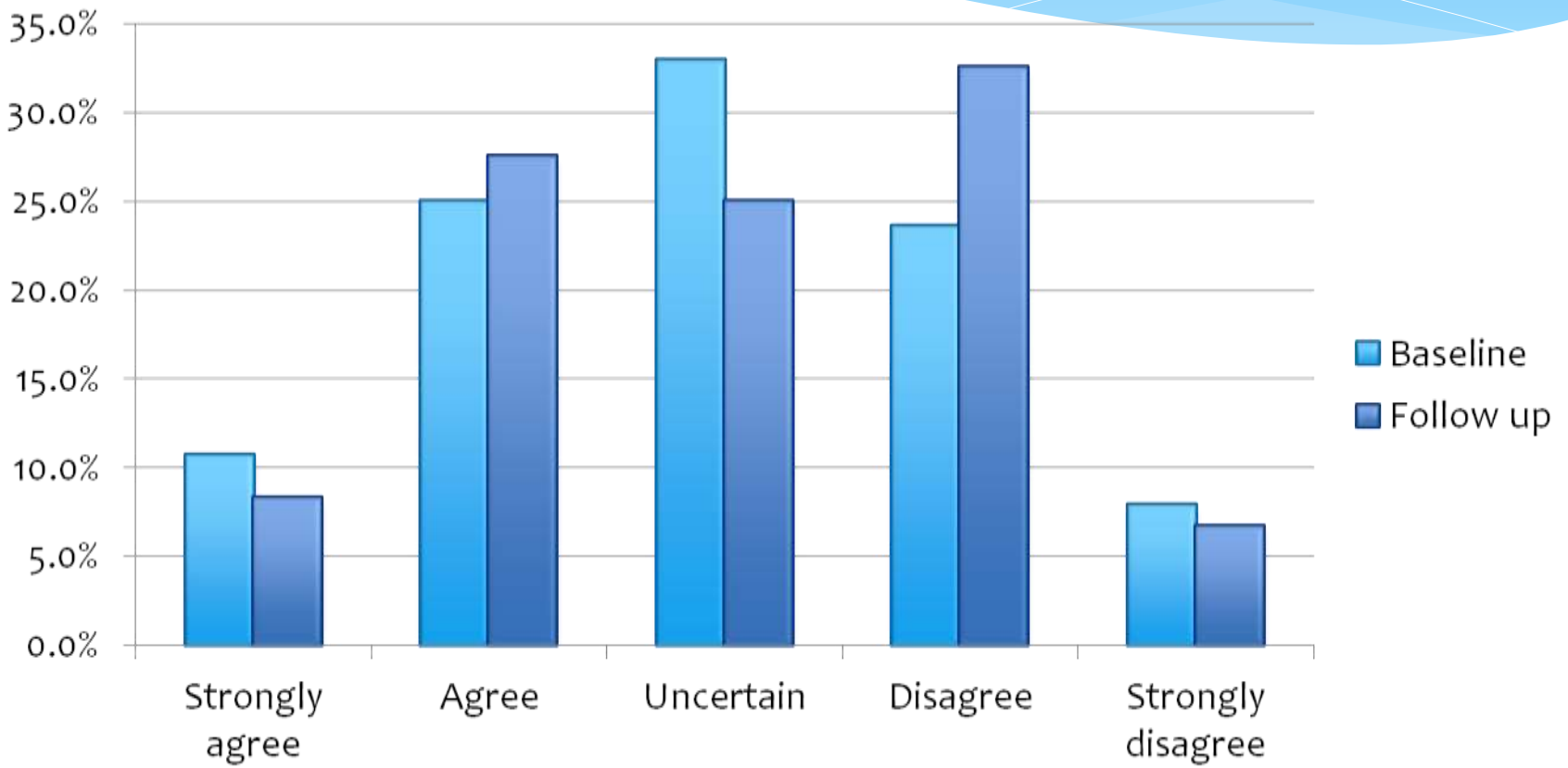
I sometimes worry about becoming too dependent on my medicines



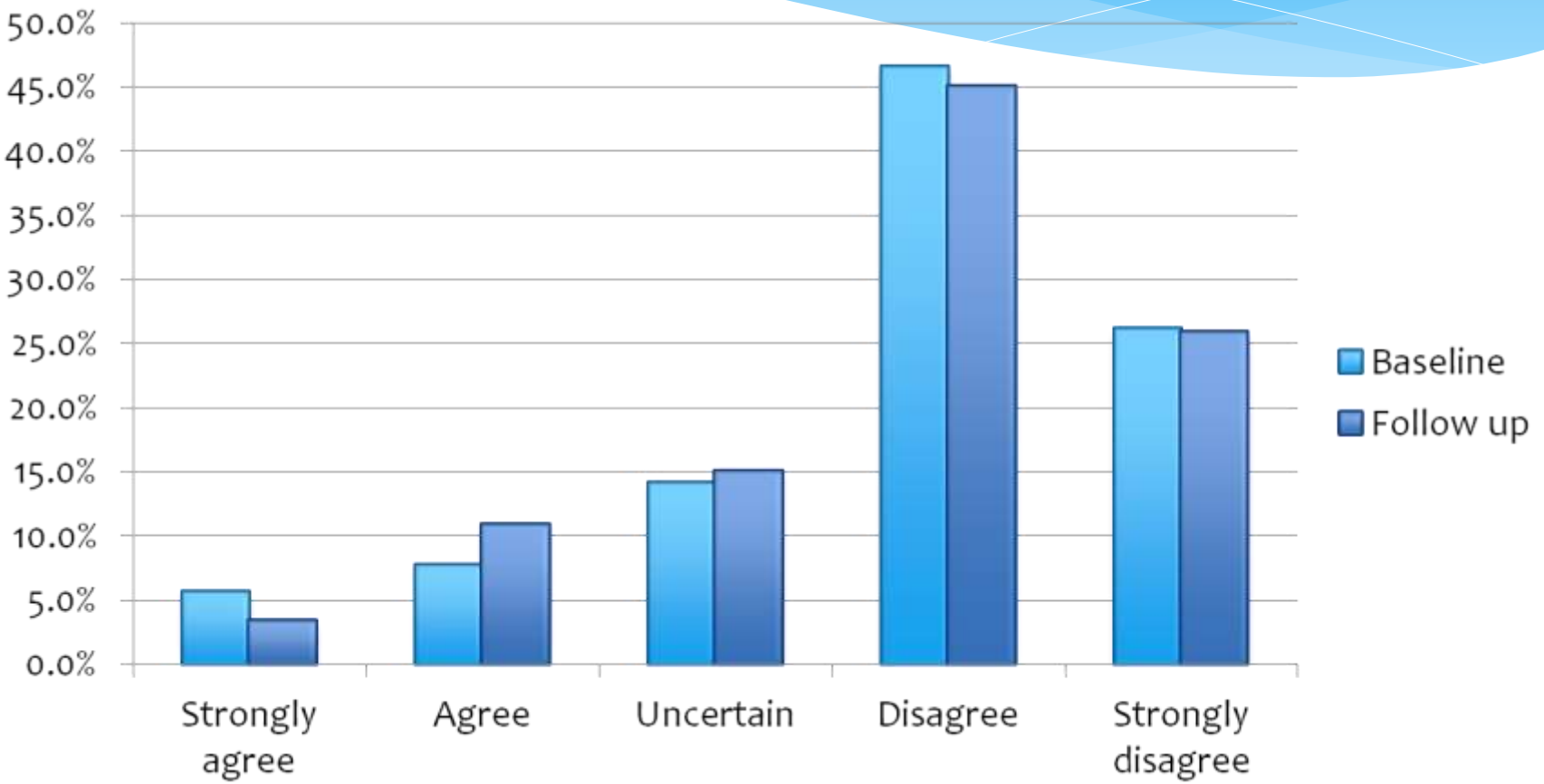
Doctors use too many medicines



If doctors had more time with patients they would prescribe fewer medicines



People who take medicines should stop their treatment for a while every now and then



Persistence with Alzheimer's medication

* The global prevalence of Alzheimer's disease (AD) is estimated to grow to more than 106 million by 2050.
* The main clinical manifestation is selective memory impairment, but also behavioural and psychological symptoms.
* Available treatments can improve symptoms and change the course of the disease in some patients.

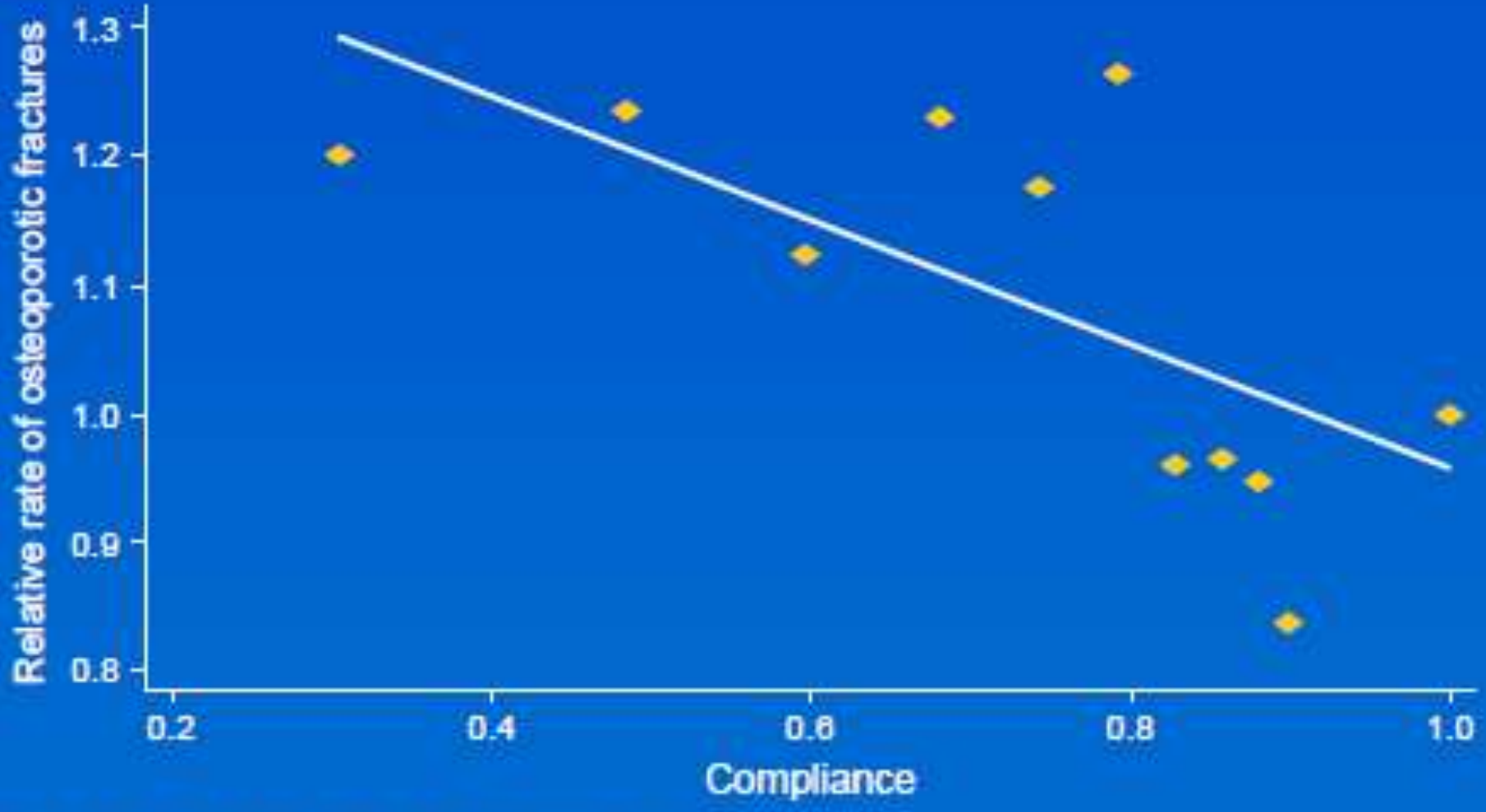
* We examined predictors of non-persistence at 6 months in a cohort of 14,197 patients initiating therapy Jan 2007-June 2010.

Brewer, Bennett, McGreevy, Williams, Eur J Clin Pharmacol 2013

Predictors of non-persistence	Hazard ratio (95 % CI)	*p* value
Male gender	0.97 (0.91–1.04)	0.41
Age 75+(vs .70–74) years	1.16 (1.06–1.27)	0.002
Medication type (vs. donepezil)		
Memantine	0.96 (0.88–1.04)	0.33
Rivastigmine	1.15 (1.03–1.27)	0.01
Galantamine	0.84 (0.73–0.96)	0.01
Year of initiation (vs. 2007)		
2008	0.90 (0.83–0.97)	0.009
2009	0.87 (0.81–0.95)	0.0013
2010	0.81 (0.73–0.89)	<0.001
Co-prescribed drugs (vs. none)		
Any antidepressant	0.89 (0.78–1.03)	0.11
Any antipsychotic	1.09 (0.93–1.28)	0.30
Polypharmacy (5+ drugs prescribed monthly)	1.08 (0.78–1.03)	0.11
Multiple vs. single anti-dementia medications	0.59 (0.54–0.65)	<0.001

Consequences of poor adherence on outcomes

Poor Adherence is Associated with Increased Risk of Fracture



Gallagher AM, et al. *J Bone Miner Res* 2008;23:1560-75.

Interventions for improving adherence

Best investment for tackling chronic diseases

* Increased adherence may lead to increasing use of treatments, but additional cost offset by savings from avoided hospitalisation and other costly interventions.
* *"Increasing the effectiveness of adherence interventions … greater impact on population health than any improvement in specific medical treatments" Haynes*

Haynes, Cochrane review

Interventions: Cochrane systematic reviews

* 10 Cochrane reviews reported interventions to improve adherence in 10 disease settings
* GOOD news: Adherence can be improved – it is a changeable behaviour
* BAD news – Previous interventions disappointing – small and short-lived improvements
* Comprehensive review for National Institute for Health research UK
  * Limitations to design of interventions and their testing
  * Failure to understand the real causes of poor adherence

1 Cochrane reviews; Gray 2009, Halpem 2008; hayes 2007; Renz 2007; Bosch-Capblanch 2007; Jordan 2006; Rueda 2006; Vermeire 2005; Schedbauer 2004, Schroeder 2004

Cochrane Collaborative: Summary of Adherence Interventions

"For long-term treatments, simplifying the dosage regimen and several complex strategies, including combinations of more thorough patient 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 can improve adherence and treatment outcomes. **If there is a common thread to these at all, it is more frequent interaction with patients with attention to adherence."**

Personalized care is essential

* Individualized – need to understand the reasons why patients are not always adherent
* Different strategies to consider:
  * Improve Drug regimen to include medication review
  * Address Patient Behaviour
    * Counseling, discuss concerns, patient reminders, special packaging
* "Identification of specific perceptual and practical barriers to adherence for each individual, both at the time of prescribing and during regular review, because perceptions, practical problems and adherence may change over time."

1NICE Clinical Guidelines on medication adherence

Take home messages

* Poor adherence is prevalent in many conditions
* Promotion of adherence leads to improved health and economic benefits.
* Adherence is influenced by many individual factors (e.g. age, comorbidity), inter-personal factors, behavioural and environmental factors
* Collaborative relationship are required in which the responsibilities and roles of both health care providers and patients are defined.
* When patients establish their own goals, they act more responsibly about controlling their disease

Personalized care should be the cornerstone of good management

Thank you

Acknowledgements: M O'Shea, Dr C Cahir, B McGowan, Dr I Barron