

A Network of Long Term Care Facilities for Conducting Pharmaco-Epi Observational Studies: Experience from USA and Europe

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Conflicts of Interest -- Mor

- F PI of NIH funded studies of long term care
- F PI of University contracts with Pharma
- F Design team of the MDS/RAI for nursing homes
- F Chair, Independent Advisory Committee on Quality for a US Nursing Home Chain
- F Founder and board member of an information services company for nursing homes



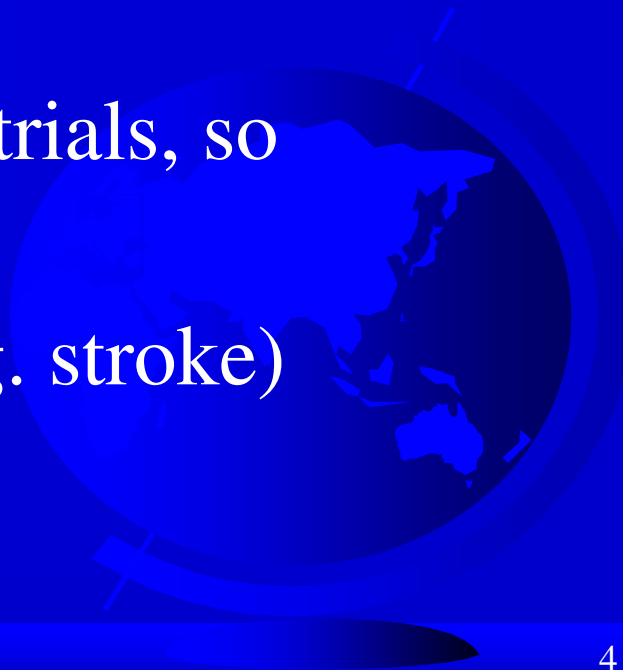
Purpose

- F Why Long Term Care Facilities?
- F Experience from U.S.
- F Experience from Europe
- F Lessons Learned
- F Conditions Necessary for Success
- F Prospects for the Future



Why Long Term Care Facilities?

- F LTCF patients use many different drugs
 - although new drugs adopted later
- F Few compliance problems; patients take all the drugs prescribed
- F These patients rarely included in trials, so important in their own right
- F High “event” rates of interest (e.g. stroke)



History of LTCF based Drug Studies

- F Early U.S. studies using computerized Medicaid drug data identified high rates of “inappropriate” drug use, negative effects of Medicaid policy changes AND identified adverse drug reactions
- F Data limitations due to lack of information on non-diagnostic confounders



Minimum Data Set (MDS) for Nursing Home Resident Assessment (RAI)

- F Mandated in U.S. from 1991
- F 300+ common data elements including function, behavior, symptoms and social & demographic information
- F Longitudinal (repeated administration)
- F Computerized in National Repository since 1999
- F Linkable to Medicare & Medicaid data

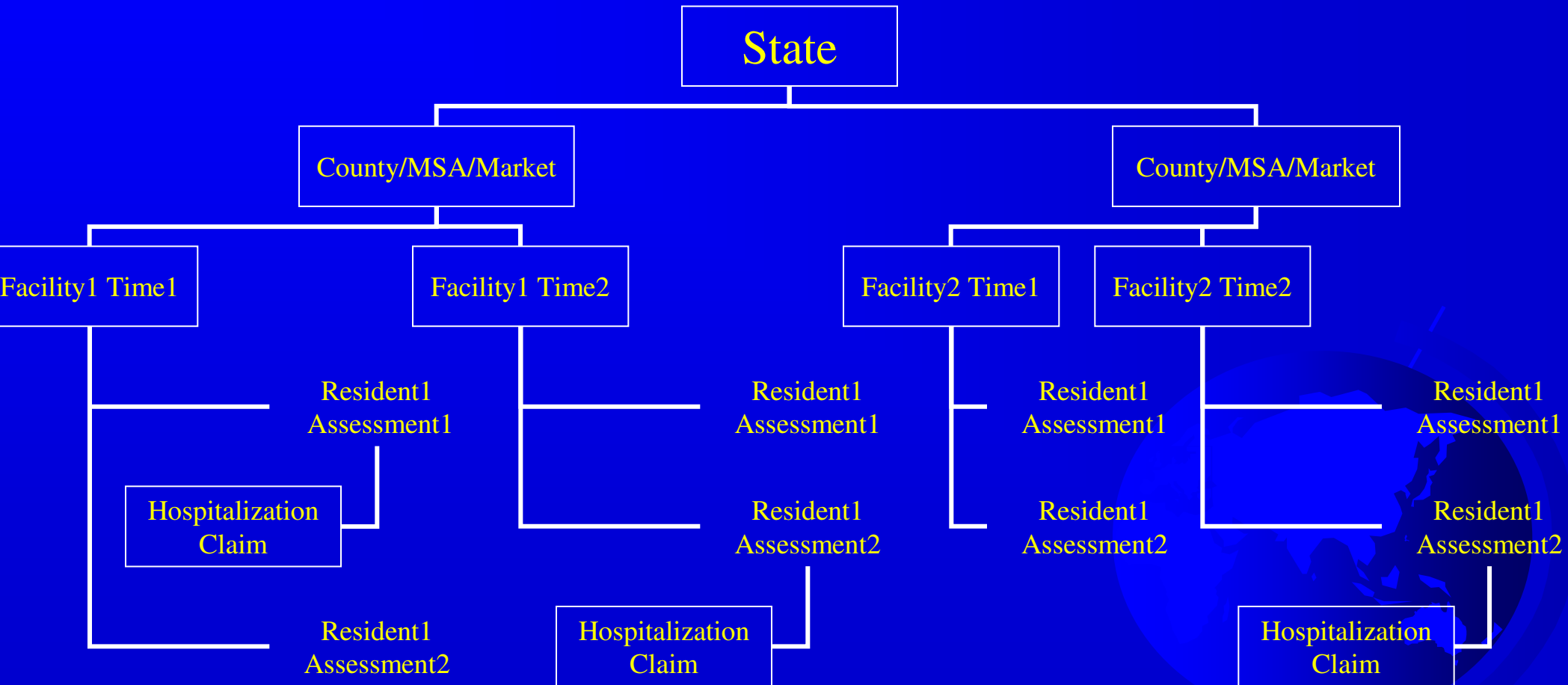


SAGE Study Group

- F In 1996, the Systematic Assessment of Geriatric drug use via Epidemiology is formed
- F International and multidisciplinary group of scientists
- F Assembled a longitudinal MDS-based data set
- F Began with Data from the Case-Mix and Reimbursement Quality Demonstration Project conducted in 5 US states between 1992-1997
- F Ultimately included MDS Repository Data on up to 9 states plus Medicare Claims



MDS Hierarchical & Longitudinal Data Relationships



SAGE Data Structure

MDS Data

Part D Drug Data

NDC codes

MULTUM

Drug Group
Drug Class
Drug Subclass
Drug Name
Drug Dosage
Drug Strength

Part D Claim

Pricing Data

CMS Data

Eligibility

Claims

Hospital
Skilled Nursing Home
Hospice
Home Health

Facility Data

Ownership
Size/ #beds
NH Chain
Staffing level
Quality deficiency
Special Care Unit

ARF Data

Census Data
Labor statistics
Health care resources

Pharmaco-Epidemiology Results

- F Extended Findings on Beneficial Effects of ACE-Inhibitors to Frail Geriatric Population
- F Tested the effect of NSAIDS on Hospitalization for Gastric Bleeds
- F Prevention of Stroke & CVD Death with Anti-Platelet and Anti-Coagulants
- F Tested Effect of Anti-Platelet and Anti-Coagulant Treatment on Bleeding
- F Examined effects of typical and atypical anti-psychotics on acute cardiac event & stroke

All-Cause Mortality Associated With Atypical and Conventional Antipsychotics Among Nursing Home Residents With Dementia: A Retrospective Cohort Study

Rosa Liperoti, MD, MPH; Graziano Onder, MD, PhD; Francesco Landi, MD, PhD; Kate L. Lapane, PhD; Vincent Mor, PhD; Roberto Bernabei, MD; and Giovanni Gambassi, MD

Objective: A recent meta-analysis has indicated that, in patients with dementia, the use of atypical antipsychotics is associated with an excess mortality. Later observational studies have suggested that conventional antipsychotics may pose an even greater risk of death. None of these studies could evaluate the risk associated with single antipsychotics nor could they provide any conclusive evidence concerning the risk among nursing home residents. We conducted a retrospective cohort study to compare the risk of death associated with atypical and conventional antipsychotics in a large population of nursing home residents with dementia.

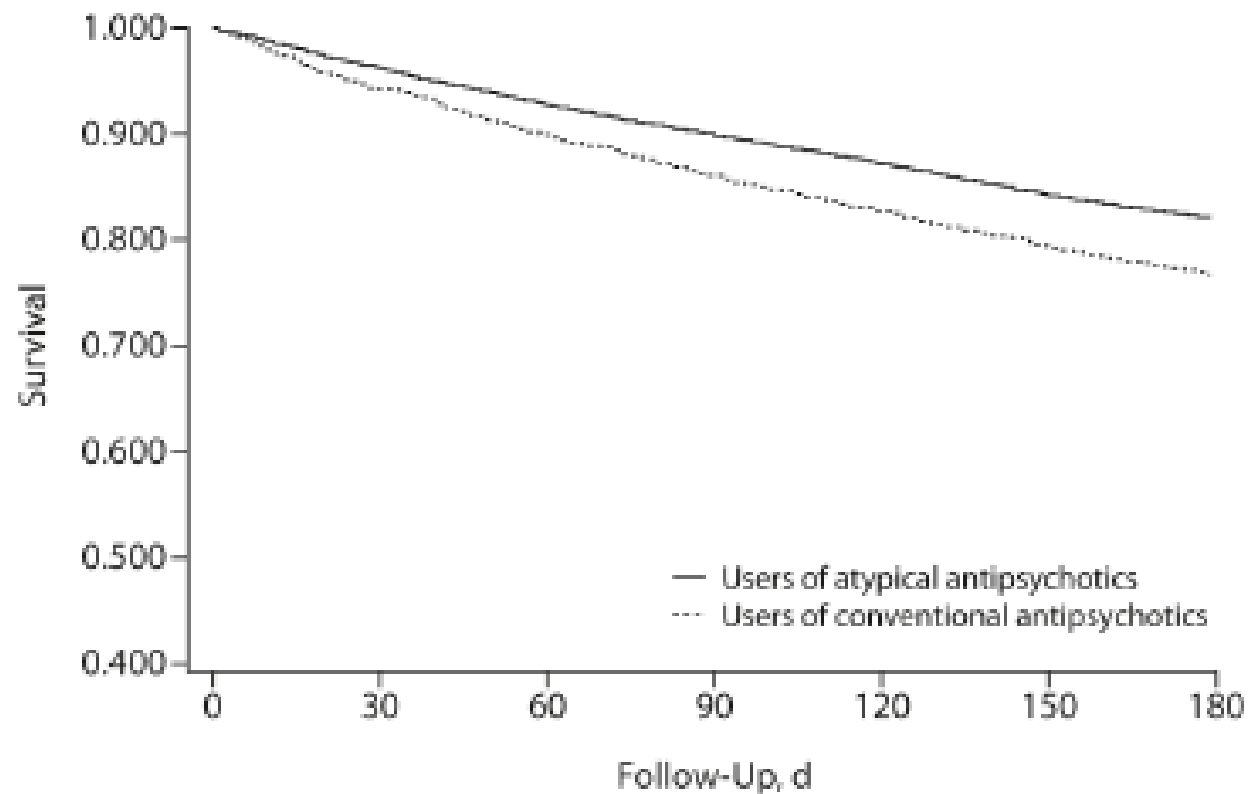
Method: We identified 6,524 new users of atypical antipsychotics and 3,205 new users of conventional antipsychotics living in 1,581 Medicare- or Medicaid-certified nursing homes in 5 US states during the years 1998–2000. The outcome measure was all-cause mortality, which was determined during 6-months of follow-up.

Results: After adjusting for potential confounders relative to users of atypicals, the rate of death was increased for users of conventional antipsychotics (hazard ratio [HR], 1.26; 95% CI, 1.13–1.42). Relative to risperidone, a higher rate of death was documented for haloperidol (HR, 1.31; 95% CI, 1.13–1.53), phenothiazines (HR, 1.17; 95% CI, 1.00–1.38) and other conventional medications (HR, 1.32; 95% CI, 0.99–1.80). No atypical antipsychotic was associated with a differential risk relative to risperidone.

Conclusions: Conventional antipsychotics are associated with a higher risk of all-cause mortality than atypical agents. It seems advisable that they are not used in substitution for atypical antipsychotics among nursing home residents with dementia even when short-term therapy is being prescribed.

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Figure 1. Survival Curves of Users of Conventional Antipsychotics and Users of Atypical Antipsychotics



Atypical users at risk, n (no. of events)	6,524 (0)	6,055 (469)	5,690 (365)	5,362 (328)
Conventional users at risk, n (no. of events)	3,205 (0)	2,881 (324)	2,652 (229)	2,461 (191)

Venous Thromboembolism Among Elderly Patients Treated With Atypical and Conventional Antipsychotic Agents

Rosa Liperoti, MD, MPH; Claudio Pedone, MD, PhD, MPH; Kate L. Lapane, PhD; Vincent Mor, PhD; Roberto Bernabei, MD; Giovanni Gambassi, MD

Background: Some antipsychotic agents have been indicated as a possible risk factor for venous thromboembolism (VTE) in adult patients with psychiatric disorders. The aim of this study was to estimate the effect of atypical and conventional antipsychotic agents on the risk of hospitalization for VTE among elderly patients.

Methods: We conducted a retrospective cohort study on nursing home residents in 5 states. We used data from the Minimum Data Set to identify 19 940 new users of antipsychotic agents and 112 078 nonusers. Hospitalization with VTE as primary discharge diagnosis was determined during a 6-month follow-up period using Medicare inpatient claims. Cox proportional hazards models provided estimates of effect adjusted for confounders.

Results: The rate of hospitalization for VTE was 0.91 per 100 person-years. Venous thrombosis accounted for 77.6%

of events and 22.4% were pulmonary embolisms. Relative to nonusers, the rate of hospitalization for VTE was increased for users of atypical antipsychotic agents, including risperidone (adjusted hazard ratio [HR], 1.98; 95% confidence interval [CI], 1.40-2.78), olanzapine (adjusted HR, 1.87; 95% CI, 1.06-3.27), and clozapine and quetiapine fumarate (adjusted HR, 2.68; 95% CI, 1.15-6.28). No increased rate was associated with phenothiazines (adjusted HR, 1.03; 95% CI, 0.60-1.77) or other conventional agents (adjusted HR, 0.98; 95% CI, 0.52-1.87).

Conclusions: Atypical antipsychotic agents appear to increase the risk of VTE. However, these events are rare, and in clinical practice the absolute risk should be weighed against the effectiveness of these medications in the elderly population.

Arch Intern Med. 2005;165:2677-2682

Table 4. Effect of Antipsychotic Drug Use on the Risk of Hospitalization for VTE Among Residents Without Major Risk and Protective Factors for VTE Among Residents With Minimal or Moderate Cognitive Impairment

Agent	Adjusted HR (95% CI)	
	Residents Without Main Risk and Protective Factors for VTE (n = 88 441)*	Residents With Minimal or Moderate Cognitive Impairment (CPS Score ≤3) (n = 98 370)†
Atypical agents	2.43 (1.69-3.49)	1.94 (1.33-2.58)
Risperidone	2.54 (1.69-3.82)	1.83 (1.23-2.72)
Olanzapine	1.71 (0.96-3.45)	1.95 (1.06-3.62)
Clozapine–quetiapine fumarate	4.88 (2.03-11.72)	2.79 (1.09-7.13)
Conventional agents	1.00 (0.57-1.78)	0.90 (0.56-1.44)
Phenothiazines	0.96 (0.56-2.02)	1.00 (0.56-1.79)
Other	1.04 (0.45-2.40)	0.77 (0.36-1.64)
>1 Antipsychotic agent	5.29 (2.05-13.66)	2.82 (1.01-7.90)
Nonusers	Referent	Referent

Abbreviations: CI, confidence interval; CPS, Cognitive Performance Scale; HR, hazard ratio; VTE, venous thromboembolism.

*Main risk factors for VTE included history of deep venous thrombosis, history of hip fracture, cancer, use of anticoagulants, and use of estrogens. These HRs were adjusted for age, sex, body mass index, activities of daily living score, CPS score, chronic obstructive pulmonary disease, dementia, depression, peripheral vascular disease, cerebrovascular disease, heart failure, diabetes mellitus, and use of aspirin or antiplatelets.

†These HRs were adjusted for age, sex, body mass index, activities of daily living score, CPS score, history of deep venous thrombosis, history of hip fracture, chronic obstructive pulmonary disease, cancer, dementia, depression, peripheral vascular disease, cerebrovascular disease, heart failure, diabetes mellitus, and concomitant drug use, including anticoagulants, aspirin or antiplatelets, and estrogens.

Early Cross-National Comparisons of Drug Use

- F Promulgation of the MDS/RAI to other countries made possible simple comparisons of the characteristics of nursing home residents
- F Selected only countries with data on ALL facilities in an area/region and each participating country aggregated data to the level of the nursing home to allow comparison of anti-psychotic drug use rates



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Int J Geriatr Psychiatry 2009; 24: 1–9.

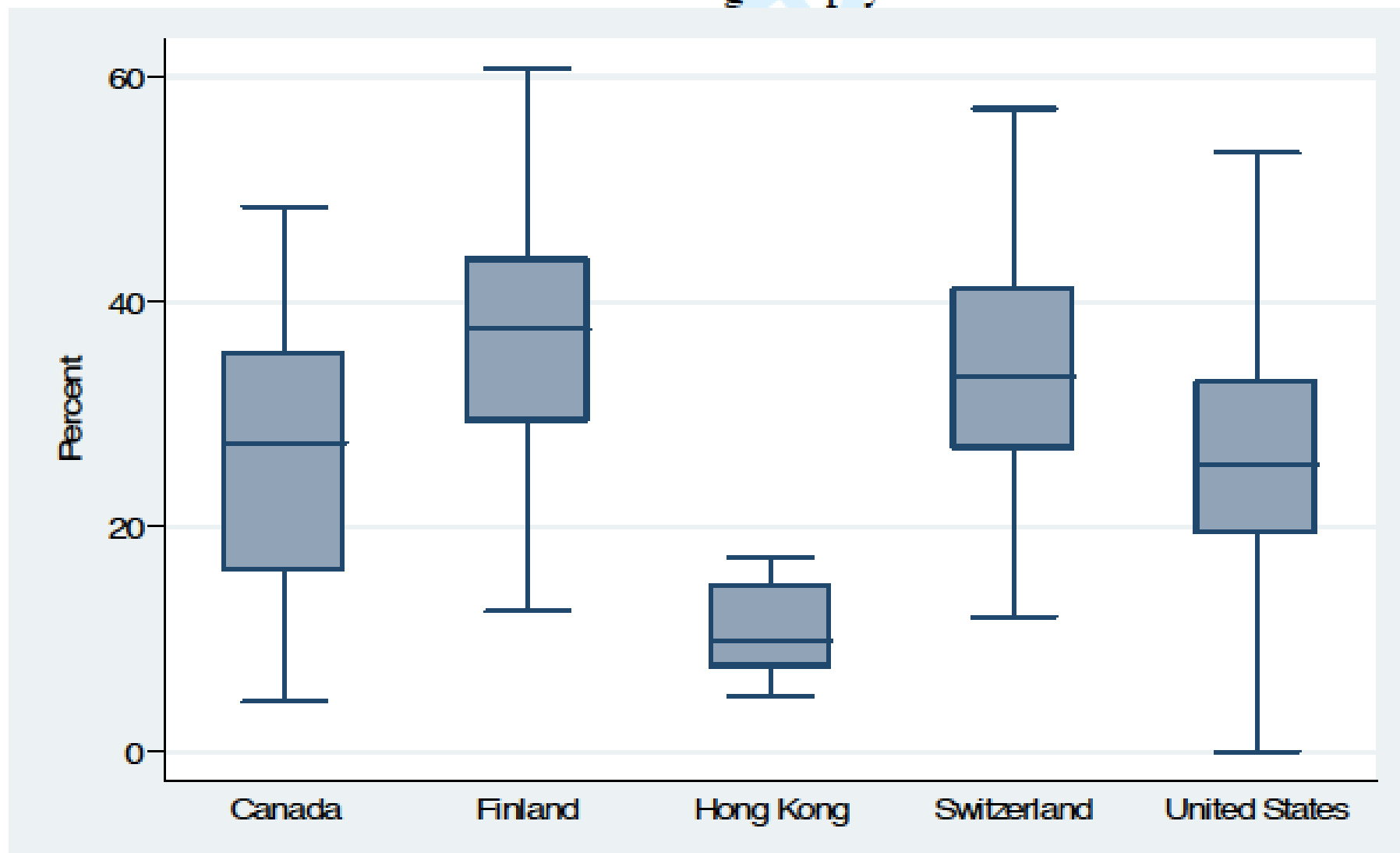
Published online in Wiley InterScience

(www.interscience.wiley.com) DOI: 10.1002/gps.2232

Use of physical restraints and antipsychotic medications in nursing homes: a cross-national study

Zhanlian Feng^{1*}, John P. Hirdes^{2,3}, Trevor F. Smith⁴, Harriet Finne-Soveri⁵, Iris Chi⁶, Jean-Noel Du Pasquier⁷, Ruedi Gilgen⁸, Naoki Ikegami⁹ and Vincent Mor¹⁰

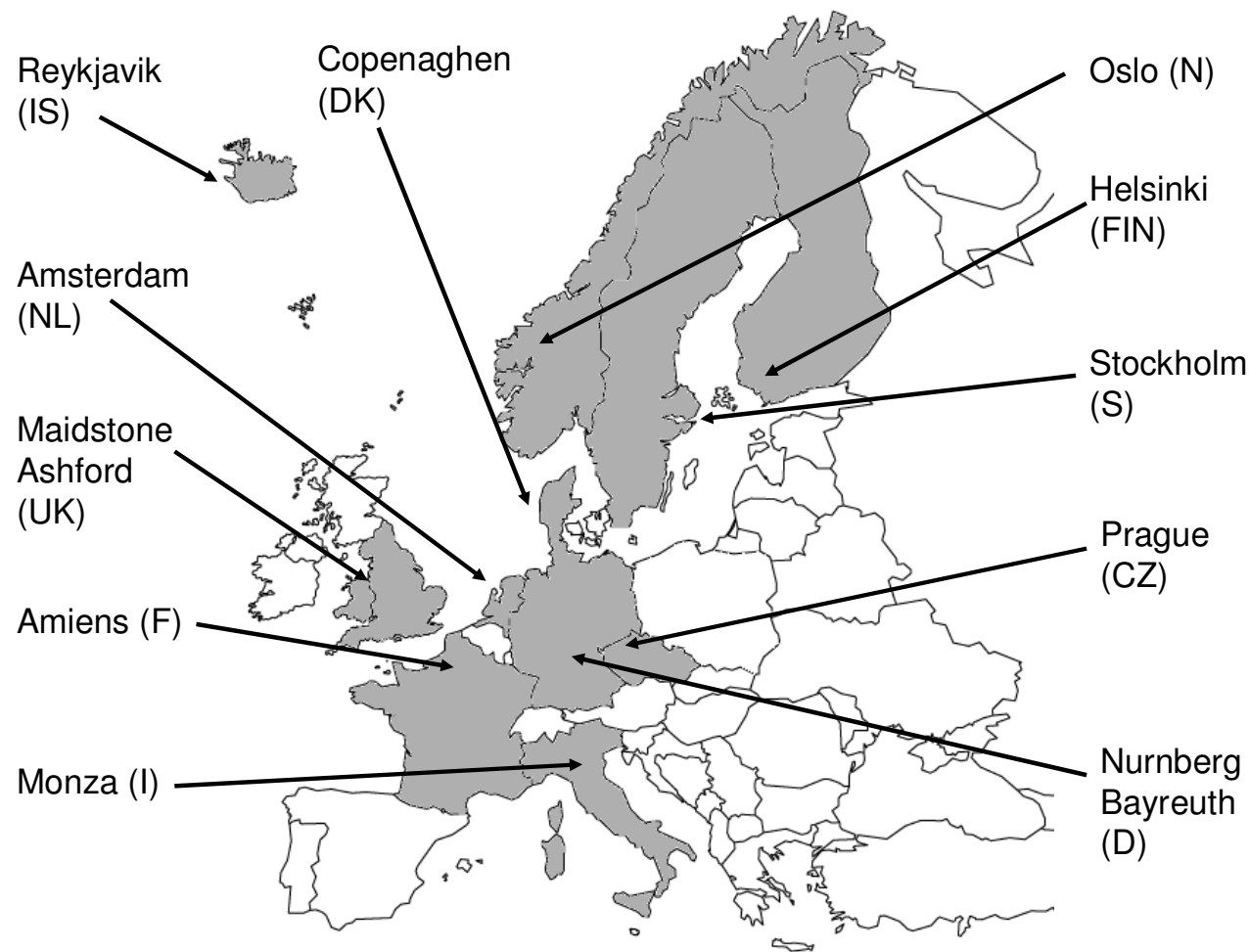
B. Percent Residents Receiving Antipsychotic Medications



Note: In each country, extreme values (outliers) exceeding ± 1.5 times the interquartile range were excluded from the box plot.

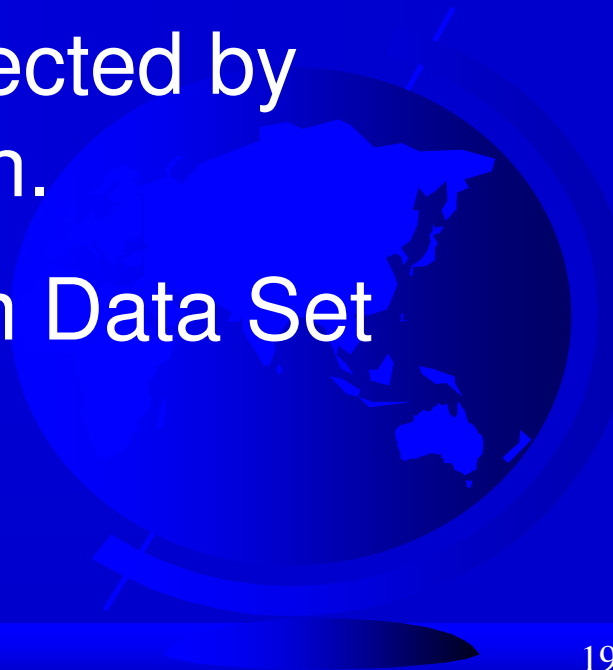
Developing an evidence-base for community care services in Europe

The Aged Home Care project ADHOC



AdHoc study

- F 4007 subjects in Home Care in 11 European countries;
- F Age \geq 65 years;
- F At each site subjects were selected by computer-driven randomisation.
- F Data collected by the Minimum Data Set for Home Care version 2.0.

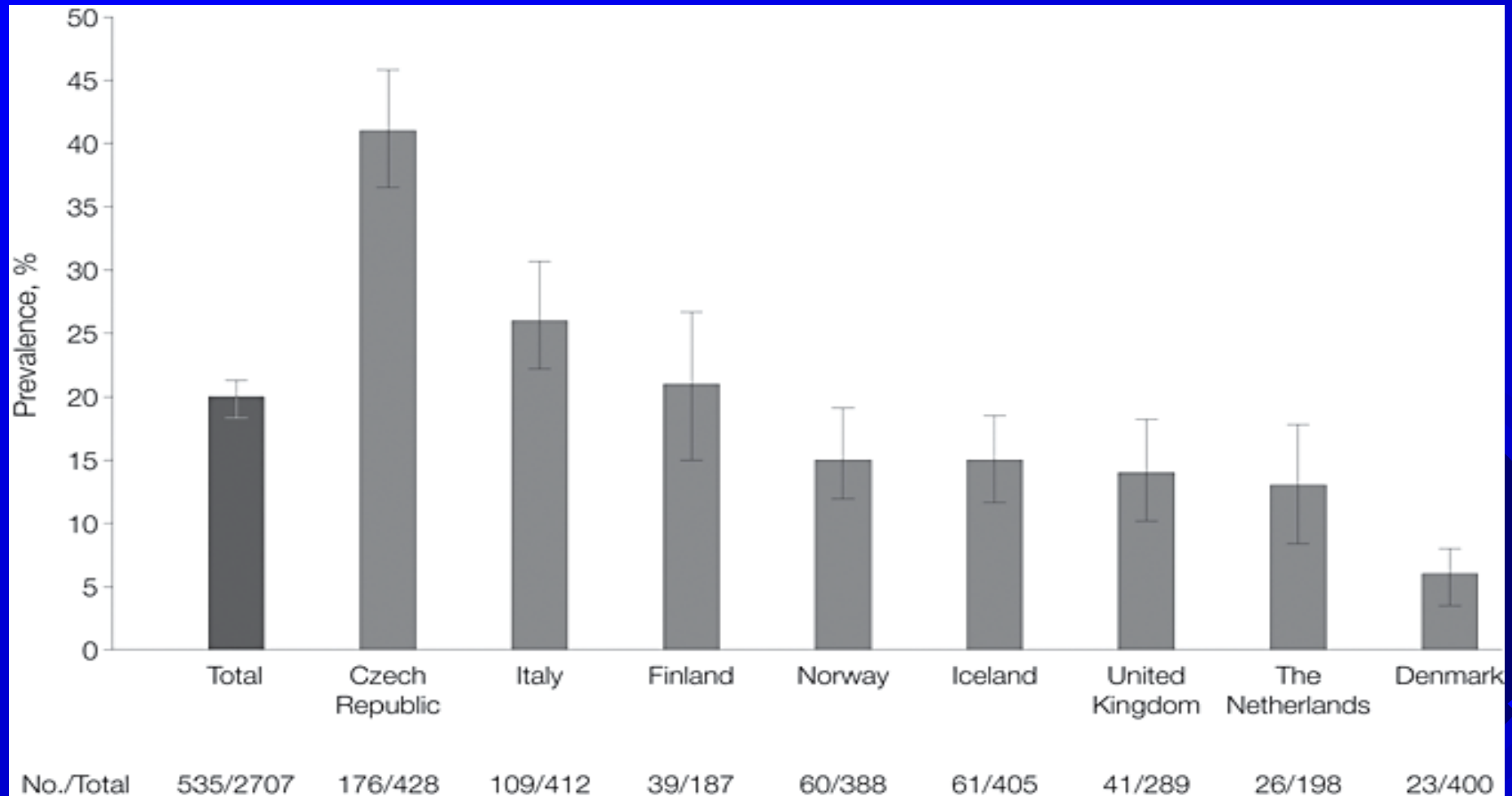


AD-HOC Objectives

- F Description and comparison of the characteristics of patients in each European HC Service;
- F Identification at the patient-level and at the system-level of the independent predictors of positive or negative outcomes;



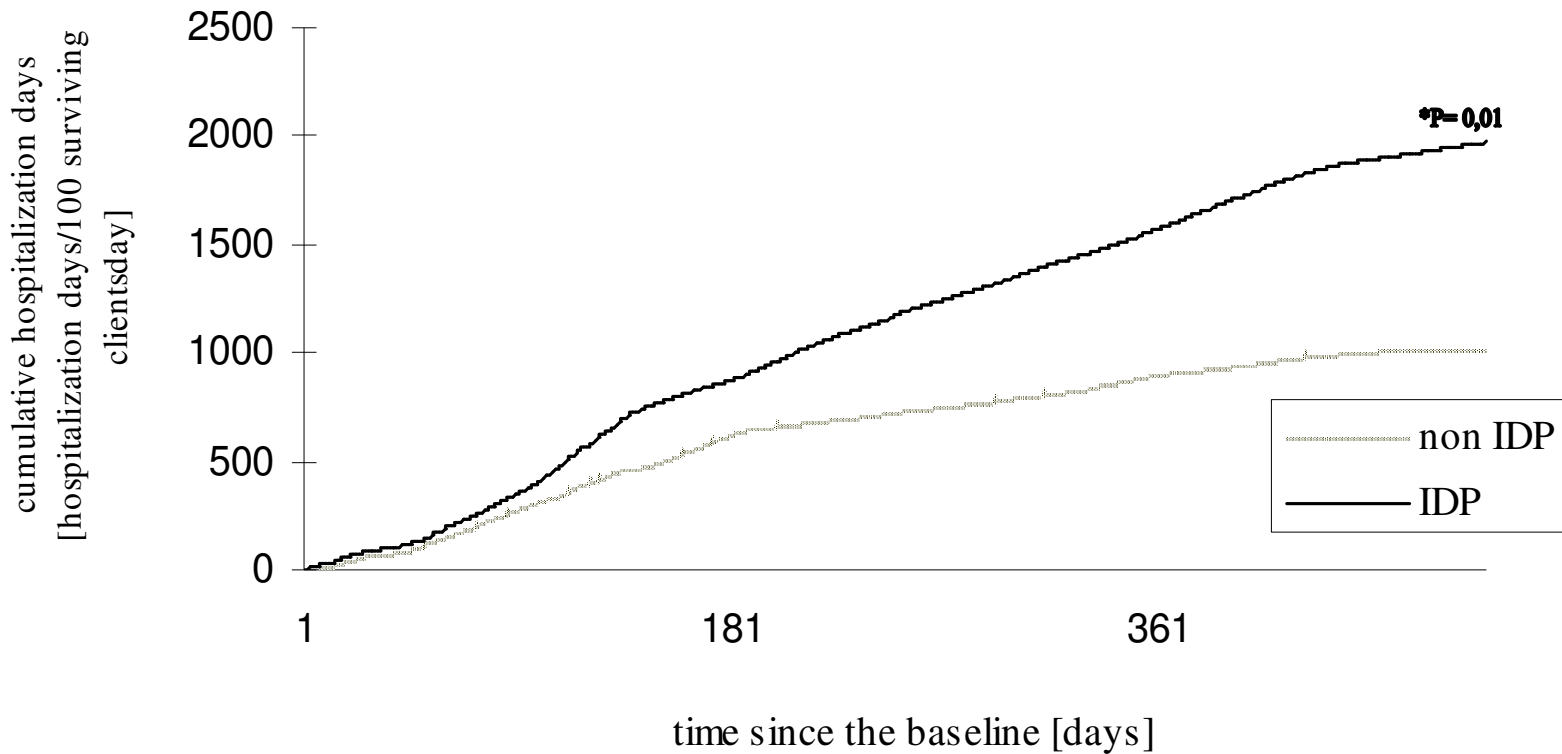
Prevalence of Potentially Inappropriate Medication Use Considering All Explicit Criteria Combined (Beers 1997, Beers 2003, and McLeod 1997)



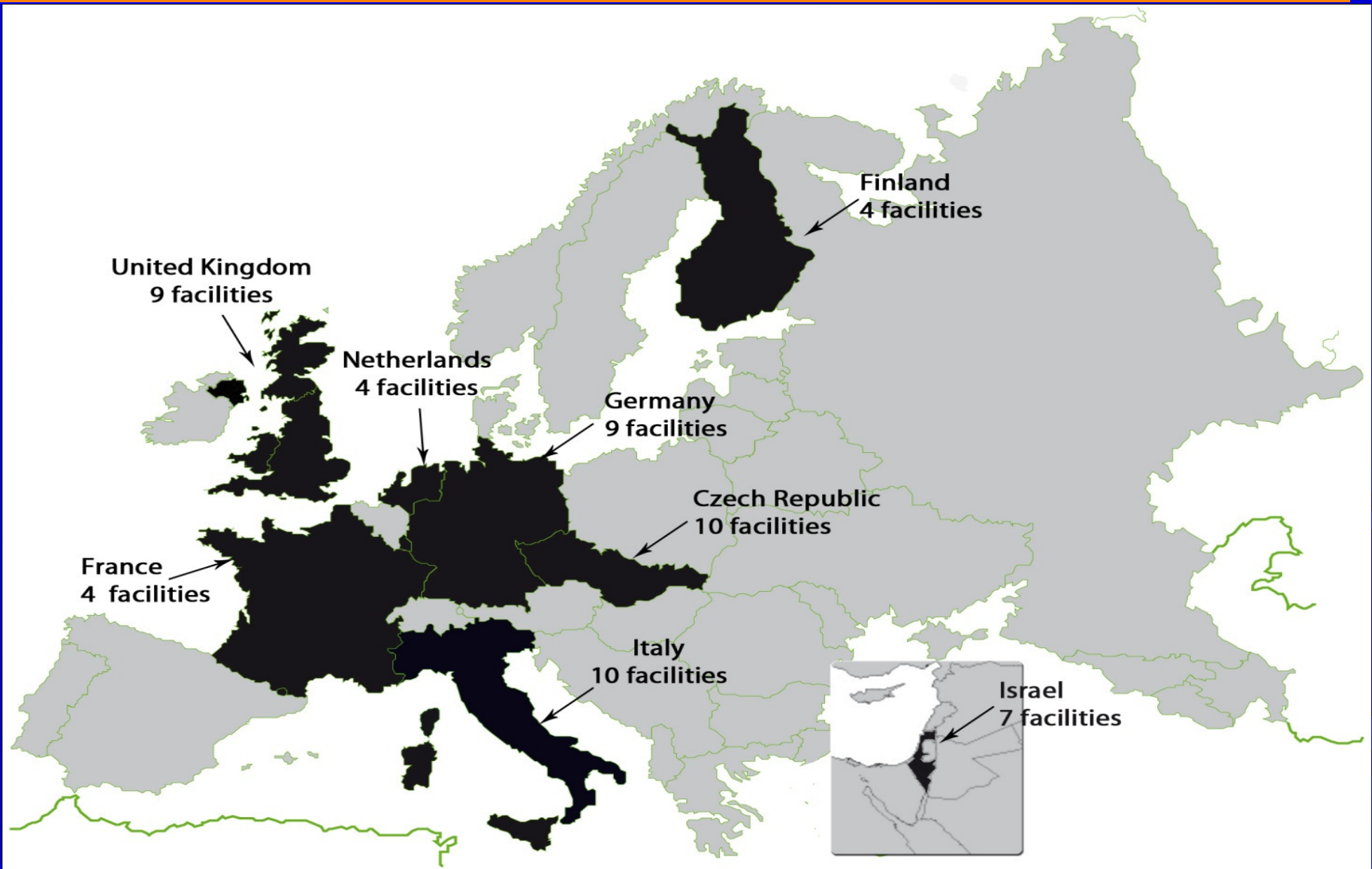
Fialova, D. et al. JAMA 2005

1- Year Cumulative Acute Hospitalization Days in inappropriate drug users and nonusers

(ADHOC project, Prague HC clients, the baseline period: Sept 2001- Jan 2002)



SHELTER – participating countries



Study objective:

To validate the InterRAI-LTCF as a methodology to assess the provision of care in NH in Europe

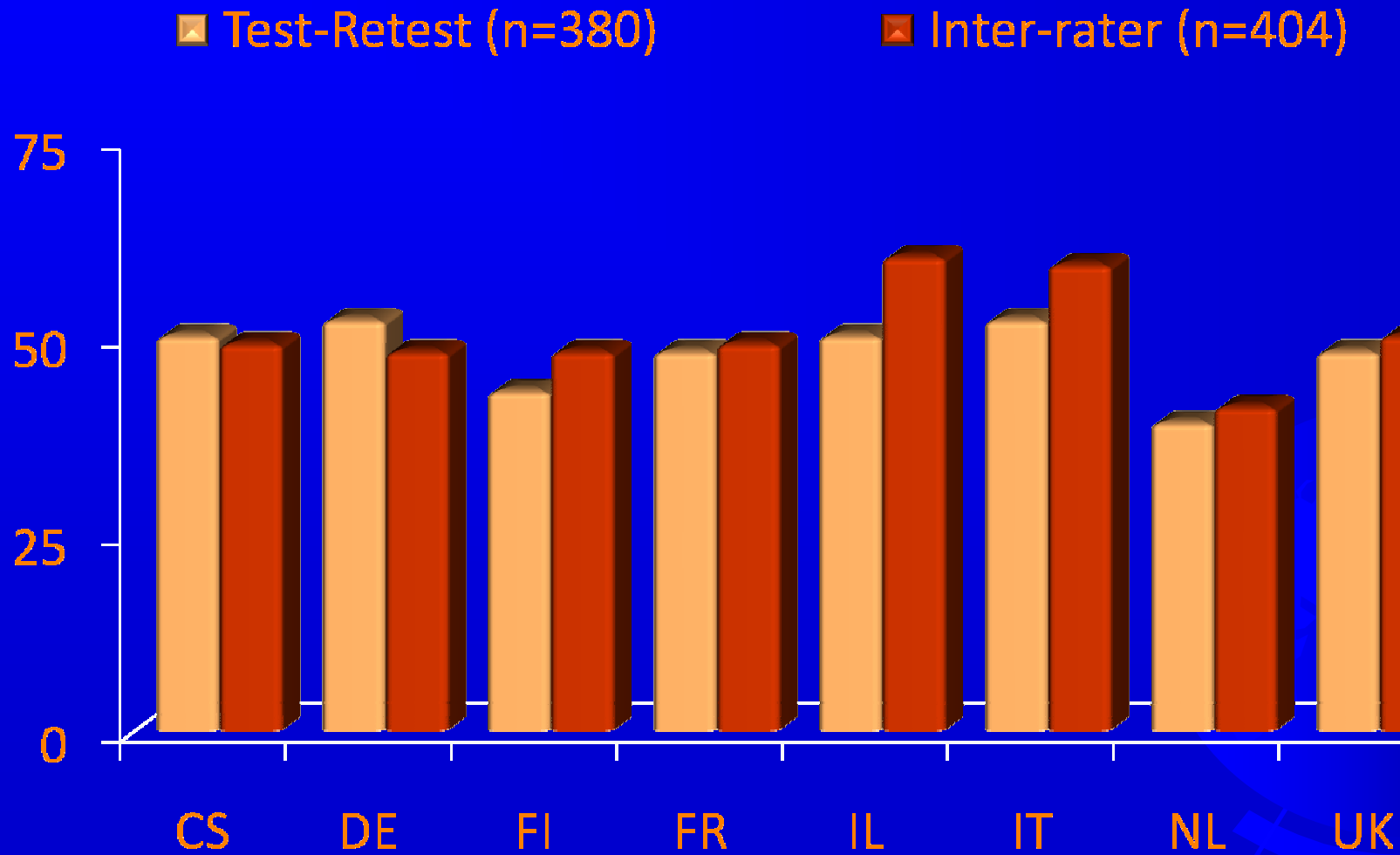
First step: Linguistic Validation

Second Step: Face Validity Assessment

Third Step: Inter-rater & test-retest Reliability



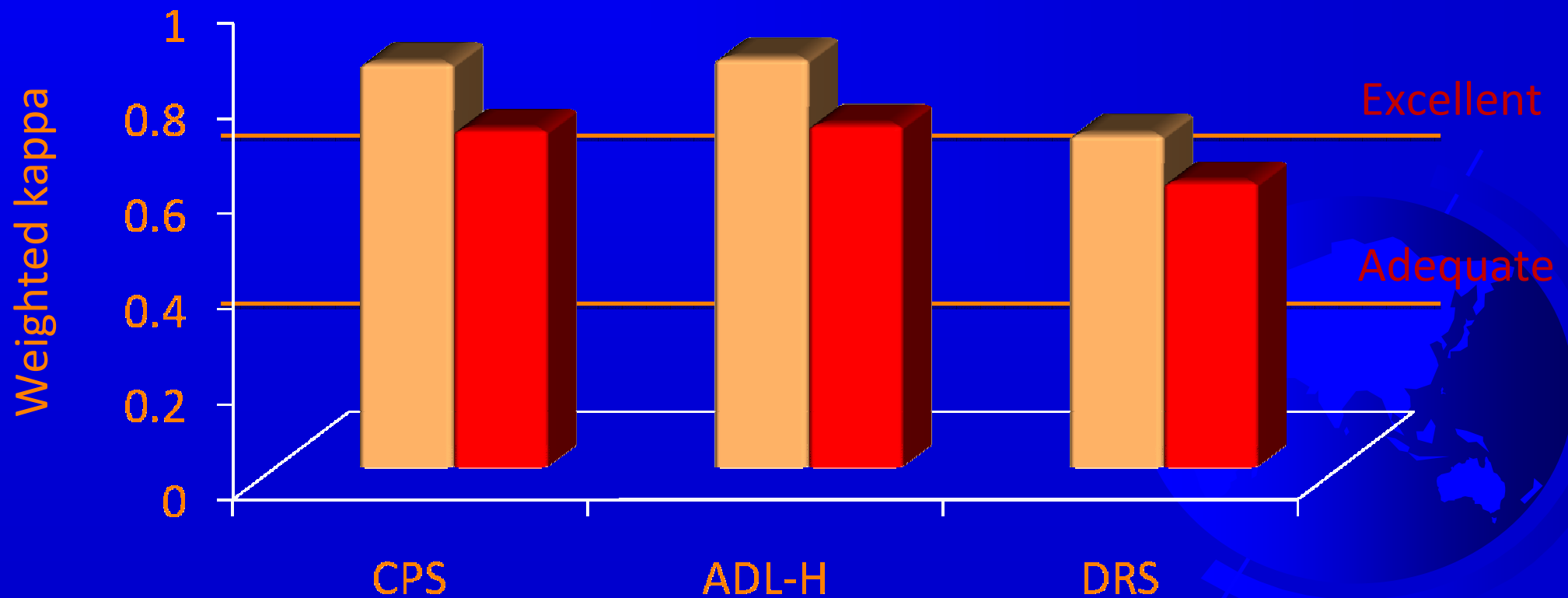
Reliability – sample



Reliability - Scales

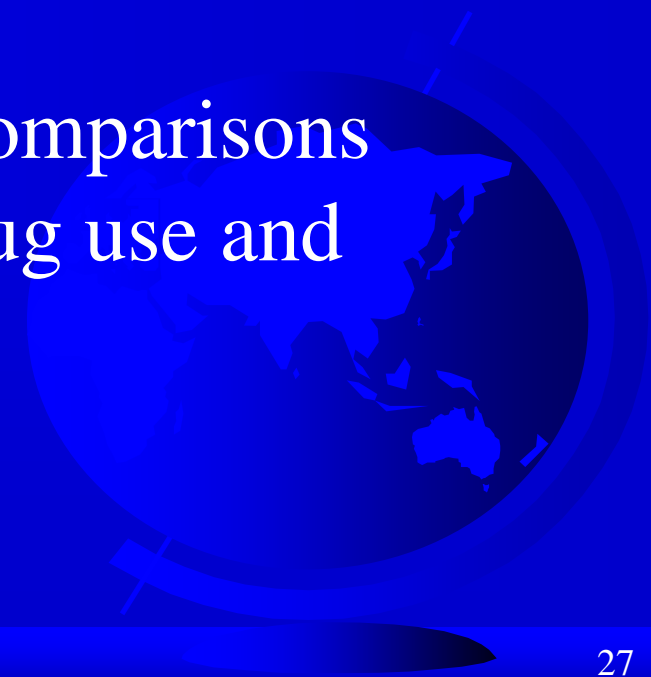
Test-Retest

Inter-rater



SHELTER Drug Use Data

- F All current medications collected in all nursing home residents
- F Examinations of cross-country comparisons of drug use patterns underway
- F Examinations of cross-country comparisons as to the relationship between drug use and patient characteristics underway



Qualities of an Effective Provider Network for Observational Pharmaco-Epi Studies

- F Population of Providers in a Region/State
- F Longitudinal Clinical/Diagnostic Patient Data
- F Socio-demographic & updated functional data
- F Complete & Uniform Ascertainment of Outcome Events (death (cause); hospitalization (diagnoses))
- F Drug prescription data (date, detail, dose, route)
- F Provider characteristics (size, staffing, etc.)

Challenges in Interpreting Data from LTCF Networks

- F Multi-morbidity creates lots of background noise
- F Complicated confounding by indication at patient and facility levels
- F Assumes common hospitalization decision rules to assess patient outcomes (or use of facility fixed effects)
- F Likely correlation between poor prescribing and poor quality of care, unrelated to drugs



Advantages of LTCF Network Outweigh Disadvantages

- F Challenges of Provider effects complicating interpretation present in ALL pharmaco-epi studies since Dartmouth studies reveal Physician or hospital effects are strong
- F Only way at present to have any data on effects of drugs on the population that uses most drugs
- F Have the potential to be used for cluster random assignment trials



Summary

- F U.S. experience in building a network of LTCFs with data on drug exposure, morbidity and outcomes made possible by regulatory mandates
- F European and other international settings could adopt the same approach but requires uniform data and considerable analytic sophistication to deal with inevitable errors

