Intensity of Warfarin Therapy and Use of Interacting Medications in Long-Term Care

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Inspiring Innovation and Discovery

Background

- Warfarin is the most commonly used form of oral anticoagulation

- Intensity of anticoagulation monitored with International Normalized Ratio (INR)
  - Narrow therapeutic index
  - Variable metabolism of warfarin
  - Interacting foods and medications

Background

- Good quality evidence for optimal target INR of 2.0-3.0
  - Stroke prophylaxis in atrial fibrillation (AF)
  - Treatment of venous thromboembolism (VTE)
  - Prevention of VTE in certain high-risk patients

- Increased risk of bleeding with INR > 3.0

- Lack of clinically important anticoagulant effect with INR < 2.0

[Chest 2004; 126(6)]

Background

- Studies have found that warfarin therapy is generally poorly controlled

  [Arch Intern Med 1994; 154(17), Arch Intern Med 2000; 160(7)]

- Barriers to optimal warfarin therapy in elderly:

  1. Patient factors
     - e.g. Cognitive and functional impairment

       [Ann Pharmacother Feb 2002; 36(2), Drugs Aging 2005; 22(4)]

  2. Physician factors
     - e.g. Implementation of lower target INR

       [J Am Geriatr Soc 1997; 45(9)]

  3. Polypharmacy and high-potential for medication interaction

     [Arch Intern Med 2005; 165(10), Pharmacotherapy 2004; 24(12)]

Hypothesis

■ In long-term care facilities optimal anticoagulation should be achievable

   i.   Availability of laboratory monitoring

   ii.   Ensured adherence to warfarin therapy

   iii. Infrastructure for dose adjustment

   iv. Ability to detect all potential medication interactions

Objectives

1. To determine percentage of time in therapeutic INR range (INR 2.0-3.0)

2. To determine whether addition of a medication known to interact with warfarin was followed by INR measurement within 7 days

Study Design and Sample

- Twelve month retrospective chart review

- 5 LTCFs (total 1144 beds)

- Using the centralized pharmacy database, 107 residents on warfarin therapy were identified

- 105 residents included; 2 residents with medical indications for higher target INR excluded

Results

- Percentage of residents on warfarin = 9%

- Duration of audit
  - Mean → 9.07 months
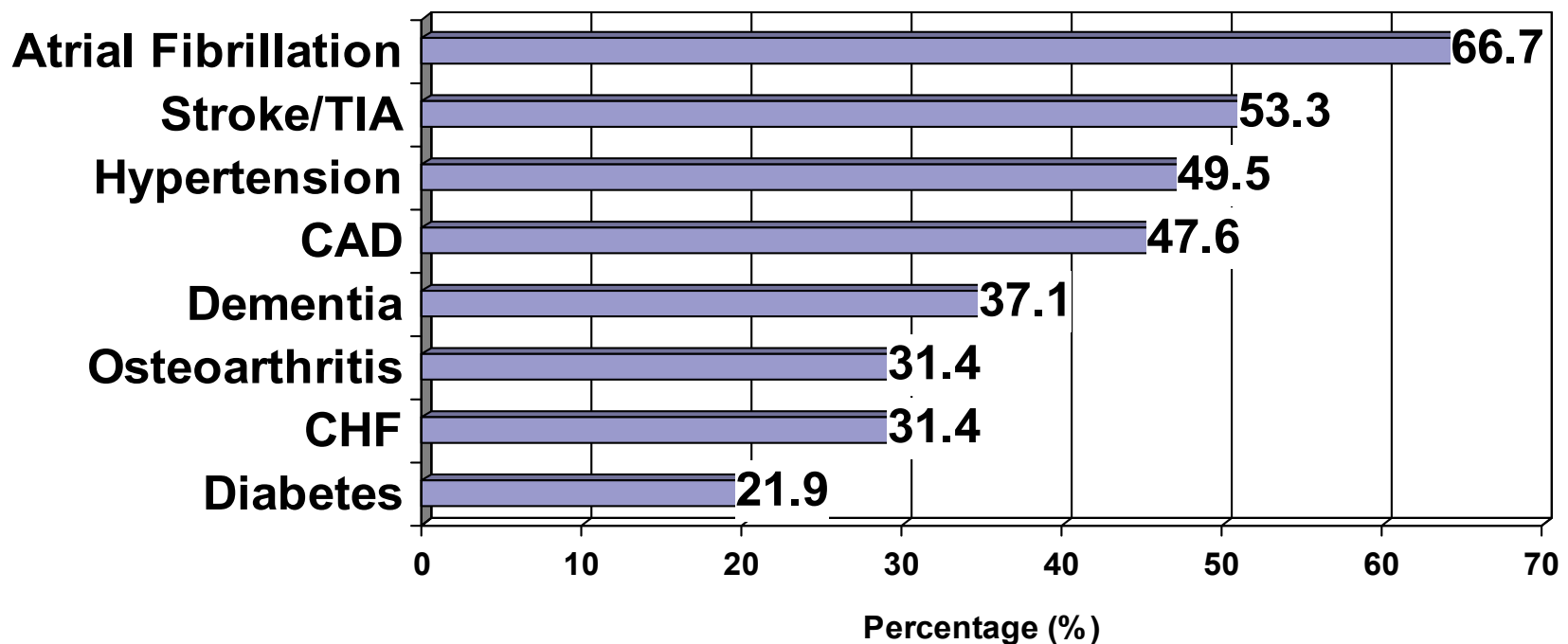 - Range → 0.7-13.3
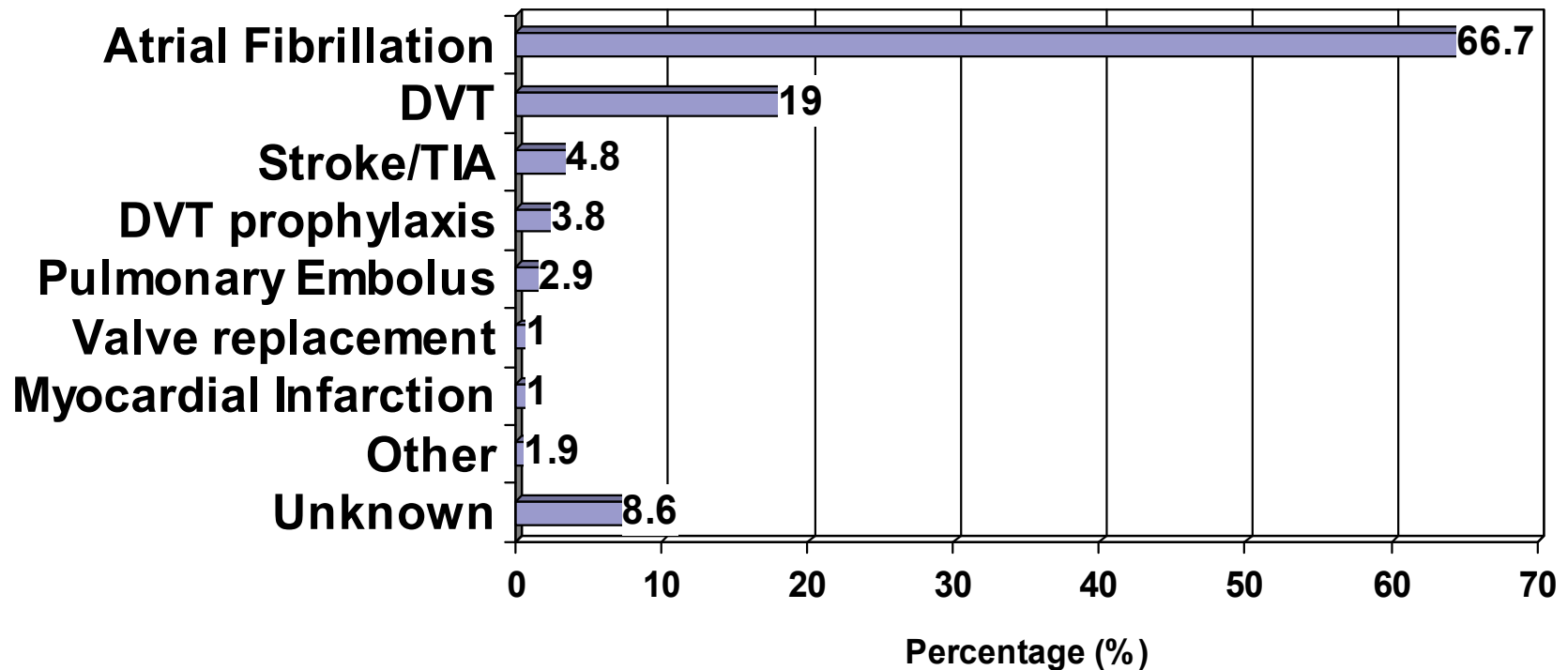 - Interquartile range → 5.8-12.1

Results - Demographics

- Gender
  - 72.4% female

- Age
  - Average $\rightarrow$ 83.6 yrs
  - Range $\rightarrow$ 54.7-98.0 yrs

- BMI (kg/m^2)
  - Average $\rightarrow$ 24.9
  - Range $\rightarrow$ 14.8-37.9

Prevalence of Major Comorbidities in Sample

Comorbidity	Percentage (%)
Atrial Fibrillation	66.7
Stroke/TIA	53.3
Hypertension	49.5
CAD	47.6
Dementia	37.1
Osteoarthritis	31.4
CHF	31.4
Diabetes	21.9

Percentage (%)

Indications for Warfarin

Percentage (%)

- Proportion (%) with one indication → 95/105 (90.5%)
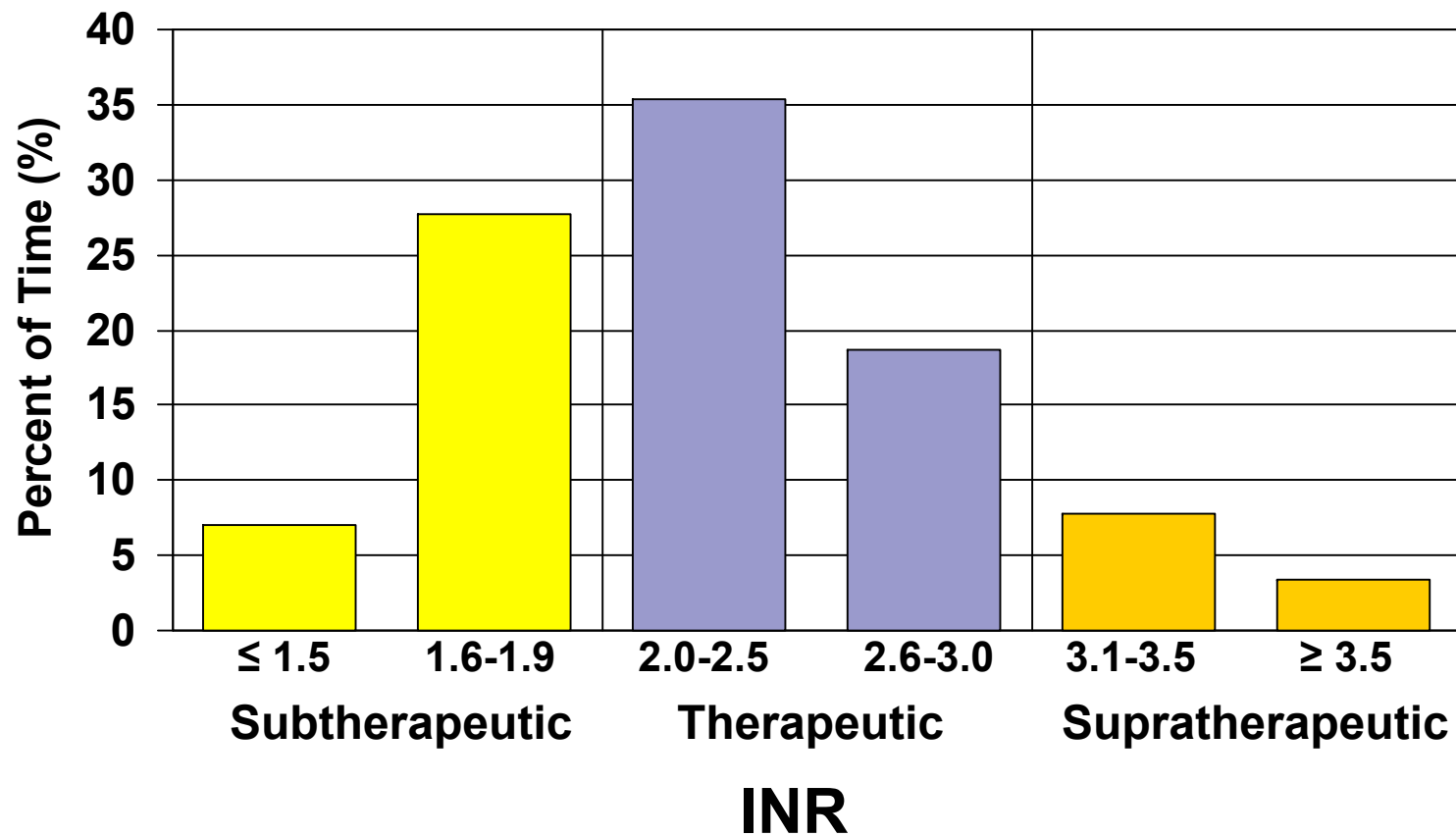- Proportion (%) with two indications → 10/105 (9.5%)

INR

- Total of 3065 INR values available, representing 28,310 resident-days

- Average number of INR measurements per resident per month = 3.4

- Time in therapeutic range (TTR) calculation
  - Linear interpolation of INR values

Overall:
# Time in Therapeutic Range
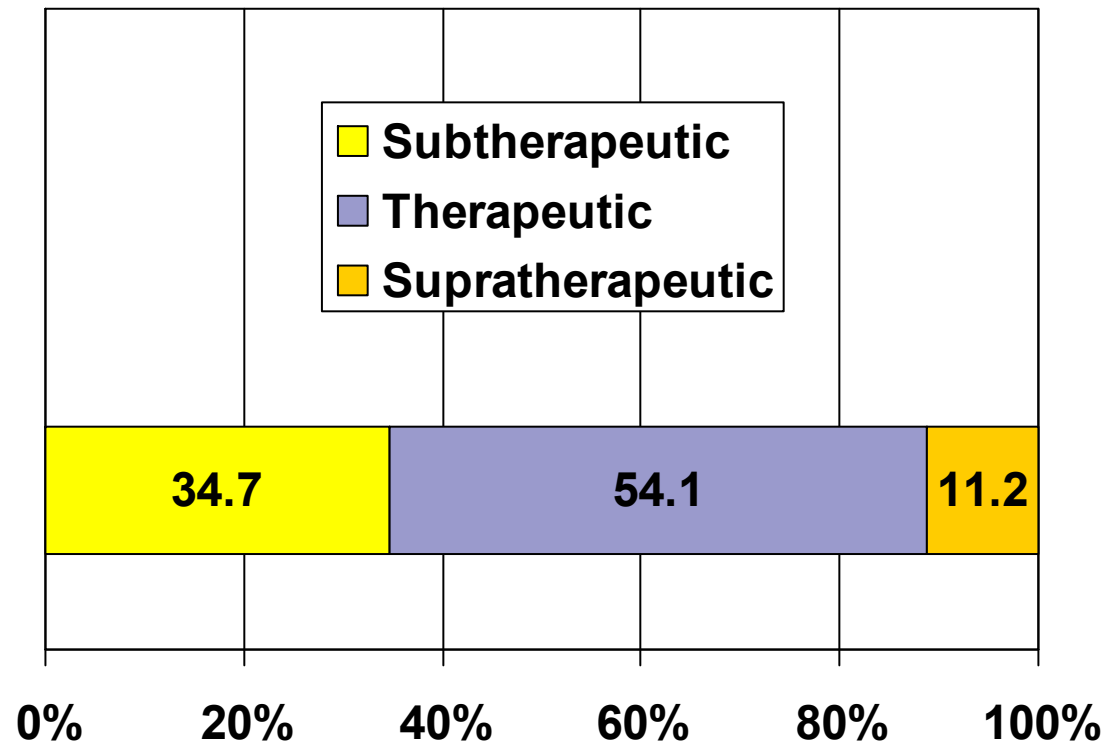
# Time in the Therapeutic Range (TTR)

Interacting Medications

- Pharmacy database for these residents searched for prescription of medications known to interact with warfarin

- List of medications based on "highly probable" and "probable" interactions in recent systematic review [Arch Intern Med 2005; 165(10)]

Interacting Medications

Medication	No. (%)
Acetaminophen	42 (40%)
Citalopram	26 (25%)
Acetylsalicylic acid	17 (16%)
Diltiazem	12 (11%)
Simvastatin	10 (10%)
Levofloxacin	8 (8%)
Phenytoin	7 (7%)
Ciprofloxacin	5 (5%)
Sertraline	5 (5%)
Cotrimoxazole	3 (3%)
Metronidazole	3 (3%)
Clarithromycin	3 (3%)
Amiodarone	3 (3%)
Amoxicillin-clavulinate	2 (2%)
Miconazole	1 (1%)
Propranolol	1 (1%)
Fluvoxamine	1 (1%)
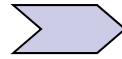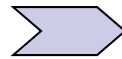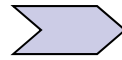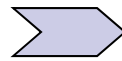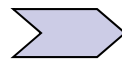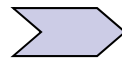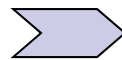
Interacting Medications

- 79% of residents (83 residents) were prescribed at least one interacting drug during period of chart audit

  - Average of 1.8 interacting medications per resident over duration of chart review (range 1-6)

Interacting Medications

- 72 instances of newly initiated medications or dosage changes

- Was INR checked within ≤7 days after initiation of medication or change in dose?
  - Yes – 59/72 (81.9%)

Conclusions

- INR was in therapeutic range 54.1% of time

- INR was subtherapeutic over one-third of time

- Majority of residents were on medications known to interact with warfarin

- 20% of the time, INR was not measured within ≤7 days after initiation or change in medication dose

Dosing Algorithm

- One dosing algorithm has previously been validated in patients in the community

- Found to result in INR 2.0-3.0 in more than 80% of cases [NEJM 2003; 348 (12)]

- Dual use of dosing algorithm + automated interactions alerts could be studied for possible increase in ease of prescribing and improved management

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Tipps
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