

## General

### Title

Percent time in therapeutic INR range (TTR): mean TTR achieved among patients who received prescriptions for warfarin and had sufficient INR values to calculate TTR.

### Source(s)

Rose A. Staff physician, Bedford VA Medical Center. Investigator, VA Center for Health Quality, Outcomes, and Economic Research at the Bedford VA. Assistant Professor, Boston University School of Medicine. Percent time in therapeutic INR range (TTR). 2010 Oct 7. 8 p.

## Measure Domain

### Primary Measure Domain

#### Outcome

The validity of measures depends on how they are built. By examining the key building blocks of a measure, you can assess its validity for your purpose. For more information, visit the [Measure Validity](#) page.

### Secondary Measure Domain

Does not apply to this measure

## Brief Abstract

### Description

This measure is used to assess the mean therapeutic international normalized ratio (INR) range (TTR) achieved among patients who received prescriptions for warfarin and had sufficient INR values to calculate TTR.

### Rationale

Millions of patients in the United States use warfarin to prevent strokes or to prevent or treat venous thromboembolism. Warfarin is highly effective, and has been in clinical use for over 50 years. However, warfarin is difficult to manage because it has many possible interactions with diet, other drugs, and comorbid conditions that may destabilize anticoagulation control. The possible consequences of insufficient or excessive anticoagulation are extremely serious and often fatal, making it imperative to pursue good control.

The international normalized ratio (INR) test is the laboratory test used to determine the degree to which the patient's coagulation has been

successfully suppressed by the vitamin K antagonist (VKA). For most patients, the goal is to keep the INR between 2 and 3, which roughly corresponds to the blood taking 2 to 3 times as long to clot as would a normal person's blood. This level of anticoagulation has been shown to maximize benefit (i.e., protect patients from blood clots) while minimizing risk (i.e., risk of hemorrhage attributable to excessive anticoagulation). Therapeutic INR range (TTR) is a way of summarizing INR control over time.

TTR has been followed before, mostly in the setting of clinical trials where it is used to evaluate the effectiveness of warfarin therapy, particularly when warfarin is being compared to some other strategy. However, TTR has not previously been used as a quality measure – in fact, there has been a general lack of quality measurement in oral anticoagulation. There is much evidence that better anticoagulation control (i.e., higher TTR) can protect patients from severe or even fatal adverse events.

## Primary Clinical Component

Oral anticoagulation; warfarin; international normalized ratio (INR); therapeutic INR range (TTR)

## Denominator Description

All patients who received prescriptions for warfarin and had sufficient international normalized ratio (INR) values to calculate therapeutic INR range (TTR) (see the related "Denominator Inclusions/Exclusions" field)

## Numerator Description

Mean therapeutic international normalized ratio (INR) range (TTR) achieved among patients who received prescriptions for warfarin and had sufficient INR values to calculate TTR

## Evidence Supporting the Measure

### Evidence Supporting the Criterion of Quality

A clinical practice guideline or other peer-reviewed synthesis of the clinical evidence

One or more research studies published in a National Library of Medicine (NLM) indexed, peer-reviewed journal

## Evidence Supporting Need for the Measure

### Need for the Measure

Overall poor quality for the performance measured

Use of this measure to improve performance

Variation in quality for the performance measured

## Evidence Supporting Need for the Measure

Rose AJ, Berlowitz DR, Frayne SM, Hylek EM. Measuring quality of oral anticoagulation care: extending quality measurement to a new field. *Jt Comm J Qual Patient Saf.* 2009 Mar;35(3):146-55. [115 references] [PubMed](#)

Rose AJ, Hylek EM, Ozonoff A, Ash AS, Reisman JI, Berlowitz DR. Risk-adjusted percent time in therapeutic range as a quality indicator for outpatient oral anticoagulation: results of the Veterans Affairs Study To Improve Anticoagulation (VARIA). *Circ Cardiovasc Qual Outcomes.*

van Walraven C, Jennings A, Oake N, Fergusson D, Forster AJ. Effect of study setting on anticoagulation control: a systematic review and metaregression. *Chest*. 2006 May;129(5):1155-66. [97 references] [PubMed](#)

## State of Use of the Measure

### State of Use

Current routine use

### Current Use

Internal quality improvement

Quality of care research

## Application of Measure in its Current Use

### Care Setting

Ambulatory Care

Community Health Care

Home Care

Long-term Care Facilities

Managed Care Plans

Physician Group Practices/Clinics

Rehabilitation Centers

Residential Care Facilities

Rural Health Care

### Professionals Responsible for Health Care

Advanced Practice Nurses

Nurses

Pharmacists

Physician Assistants

Physicians

### Lowest Level of Health Care Delivery Addressed

Group Clinical Practices

## Target Population Age

Age greater than or equal to 18 years

## Target Population Gender

Either male or female

## Stratification by Vulnerable Populations

Unspecified

# Characteristics of the Primary Clinical Component

## Incidence/Prevalence

The number of dispensed outpatient prescriptions for warfarin in the United States (U.S.) increased from 21 million in 1998 to nearly 31 million in 2004. While there are no firm estimates for the number of patients receiving warfarin, even assuming 12 prescriptions per year for all patients, this would suggest approximately 2.5 million users in 2004, or approximately 1% of the U.S. population. In fact, patients may not receive 12 prescriptions per year (because of 90-day prescriptions and the like), so this number may be closer to 2% of the U.S. population. Also, these estimates do not account for the fact that the number of prescriptions for warfarin probably has continued to increase since 2004.

## Evidence for Incidence/Prevalence

Rose A. Staff physician, Bedford VA Medical Center. Investigator, VA Center for Health Quality, Outcomes, and Economic Research at the Bedford VA. Assistant Professor, Boston University School of Medicine. Percent time in therapeutic INR range (TTR). 2010 Oct 7. 8 p.

Wysowski DK, Nourjah P, Swartz L. Bleeding complications with warfarin use: a prevalent adverse effect resulting in regulatory action. Arch Intern Med. 2007 Jul 9;167(13):1414-9. [35 references] [PubMed](#)

## Association with Vulnerable Populations

Unspecified

## Burden of Illness

Poor anticoagulation control greatly increases the risk of stroke, venous thromboembolism (VTE), major hemorrhage, and death.

## Evidence for Burden of Illness

Connolly SJ, Pogue J, Eikelboom J, Flaker G, Commerford P, Franzosi MG, Healey JS, Yusuf S, ACTIVE W Investigators. Benefit of oral anticoagulant over antiplatelet therapy in atrial fibrillation depends on the quality of international normalized ratio control achieved by centers and countries as measured by time in therapeutic range. Circulation. 2008 Nov 11;118(20):2029-37. [21 references] [PubMed](#)

van Leeuwen Y, Rosendaal FR, Cannegieter SC. Prediction of hemorrhagic and thrombotic events in patients with mechanical heart valve

prostheses treated with oral anticoagulants. *J Thromb Haemost.* 2008 Mar;6(3):451-6. [PubMed](#)

Veeger NJ, Piersma-Wichers M, Tijssen JG, Hillege HL, van der Meer J. Individual time within target range in patients treated with vitamin K antagonists: main determinant of quality of anticoagulation and predictor of clinical outcome. A retrospective study of 2300 consecutive patients with venous thromboembolism. *Br J Haematol.* 2005 Feb;128(4):513-9. [PubMed](#)

White HD, Gruber M, Feyzi J, Kaatz S, Tse HF, Husted S, Albers GW. Comparison of outcomes among patients randomized to warfarin therapy according to anticoagulant control: results from SPORTIF III and V. *Arch Intern Med.* 2007 Feb 12;167(3):239-45. [PubMed](#)

## Utilization

Unspecified

## Costs

Events such as stroke, major hemorrhage, and venous thromboembolism (VTE) are extremely expensive to treat. In fact, stroke frequently leads to lifelong institutionalization, which is extremely expensive.

## Evidence for Costs

O'Brien CL, Gage BF. Costs and effectiveness of ximelagatran for stroke prophylaxis in chronic atrial fibrillation. *JAMA.* 2005 Feb 9;293(6):699-706. [PubMed](#)

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# Institute of Medicine (IOM) Healthcare Quality Report Categories

## IOM Care Need

Getting Better

Living with Illness

## IOM Domain

Effectiveness

## Data Collection for the Measure

### Case Finding

Users of care only

### Description of Case Finding

Patients who received prescriptions for warfarin and had sufficient international normalized ratio (INR) values to calculate therapeutic INR range

(TTR)

## Denominator Sampling Frame

Patients associated with provider

## Denominator Inclusions/Exclusions

### Inclusions

Patients who received prescriptions for warfarin and had sufficient international normalized ratio (INR) values to calculate therapeutic INR range (TTR)

Include only patients who had at least two valid intervals for calculating percent time in TTR. A valid interval consists of two INR values separated by 56 days or less, without an intervening hospitalization.

Note: All patients should be held to the standard target range of 2 to 3. If specific information is available about target ranges, it is recommended to include patients with a target range of 2.5 to 3.5, but to calculate their TTR separately.

### Exclusions

- Patients who only recorded INR values 1.2 and lower
- Patients whose primary indication to receive warfarin was valvular heart disease

Note: Refer to the articles in the "Companion Documents" field for additional details regarding the denominator inclusions/exclusions.

## Relationship of Denominator to Numerator

All cases in the denominator are equally eligible to appear in the numerator

## Denominator (Index) Event

Diagnostic Evaluation

Therapeutic Intervention

## Denominator Time Window

Time window brackets index event

## Numerator Inclusions/Exclusions

### Inclusions

Mean therapeutic international normalized ratio (INR) range (TTR) achieved among patients who received prescriptions for warfarin and had sufficient INR values to calculate TTR

### Exclusions

Unspecified

## Measure Results Under Control of Health Care Professionals, Organizations and/or Policymakers

The measure results are somewhat or substantially under the control of the health care professionals, organizations and/or policymakers to whom the measure applies.

## Numerator Time Window

Episode of care

## Data Source

Laboratory data

Pharmacy data

## Level of Determination of Quality

Not Individual Case

## Outcome Type

Clinical Outcome

## Pre-existing Instrument Used

Unspecified

## Computation of the Measure

### Scoring

Continuous Variable

### Interpretation of Score

Better quality is associated with a higher score

### Allowance for Patient Factors

Risk adjustment devised specifically for this measure/condition

### Description of Allowance for Patient Factors

The risk-adjustment model derived for this measure allows for the following variables:

- Female sex
- Age group (years): 20-54; 55-59; 60-64; 65-69; 70-74; 75+
- Race/ethnicity: Non-hispanic White; Non-hispanic Black; Hispanic; Asian; Native American; Other/Unknown
- Percentage poverty in zip code of residence (quintile): Wealthiest (0-5.9); Wealthy (5.9-9.0); Moderate (9.0-12.6); Poor (12.6-17.8); Poorest (17.8-100)
- Driving distance from nearest Veterans Administration (VA) facility in miles (quintile): Nearest (0-3.1); Near (3.1-6.0); Moderate (6.0-10.5); Far (10.5-20.3); Furthest (greater than 20.3)
- Primary indication for warfarin: Atrial fibrillation; Venous thromboembolism; All others combined
- Physical comorbid conditions: Cancer (newly diagnosed); Chronic kidney disease; Chronic liver disease; Chronic lung disease; Coronary

- artery disease; Diabetes; Epilepsy; Heart failure; Hyperlipidemia; Hypertension; Pain disorders; Peripheral arterial disease
- Mental comorbid conditions: Alcohol abuse; Anxiety; Bipolar disorder; Dementia; Major depression; Post-traumatic stress disorder; Schizophrenia; Substance abuse (non-alcohol)
- Number of non-warfarin medications: 0-7; 8-11; 12-15; 16+
- Number of hospitalizations during inception period: None; 1; 2+

Refer to the articles in the "Companion Documents" field for more details on the risk-adjustment model.

## Standard of Comparison

External comparison at a point in time

External comparison of time trends

Internal time comparison

## Evaluation of Measure Properties

### Extent of Measure Testing

A study of 124,551 patients who received outpatient oral anticoagulation from 100 Veterans Administration (VA) sites of care for indications other than valvular heart disease demonstrated that risk-adjusted therapeutic international normalized ratio (INR) range (TTR) can be used as a quality indicator for oral anticoagulation care. Risk-adjusted TTR is feasible to measure and is relatively consistent from year to year, suggesting that it is measuring an aspect of quality of care that is stable over time. This measure could be used by the VA or other integrated systems of care to profile annual performance and serve as an aid and impetus for quality improvement.

### Evidence for Reliability/Validity Testing

Rose AJ, Hylek EM, Ozonoff A, Ash AS, Reisman JI, Berlowitz DR. Risk-adjusted percent time in therapeutic range as a quality indicator for outpatient oral anticoagulation: results of the Veterans Affairs Study To Improve Anticoagulation (VARIA). *Circ Cardiovasc Qual Outcomes*. 2011 Jan 1;4(1):22-29. [PubMed](#)

## Identifying Information

### Original Title

Percent time in therapeutic INR range (TTR).

### Submitter

Rose, Adam, MD, MSc, FACP - Independent Author(s)

### Developer

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U.S. Department of Veterans Affairs, Health Services Research and Development Service, Center for Health Quality, Outcomes and Economic Research (CHQOER) - Government Affiliated Research Institute

## Funding Source(s)

U.S. Department of Veterans Affairs, Health Services Research and Development Service -- Career Development Award (to Dr. Rose)

## Composition of the Group that Developed the Measure

Adam Rose, MD, MSc, FACP; Elaine Hylek, MD, MPH (Boston University School of Medicine, Section of General Internal Medicine); Al Ozonoff, PhD (Boston Children's Hospital, Biostatistics); Arlene Ash, PhD (University of Massachusetts School of Medicine); Joel Reisman (Statistical Programmer, Bedford VA Medical Center); Dan Berlowitz, MD, MPH (Bedford VA Medical Center, Boston University School of Medicine, Boston University School of Public Health, Department of Health Policy and Management)

## Financial Disclosures/Other Potential Conflicts of Interest

Dr. Hylek has received honoraria from Bayer and Bristol-Myers Squibb, and has served on advisory boards for Boehringer-Ingelheim, Bristol-Myers Squibb, Merck, and sanofi-aventis. None of the other developers of this measure report any potential conflicts of interest.

## Adaptation

Measure was not adapted from another source.

## Release Date

2010 Jul

## Revision Date

2011 Jan

## Measure Status

This is the current release of the measure.

## Source(s)

Rose A. Staff physician, Bedford VA Medical Center. Investigator, VA Center for Health Quality, Outcomes, and Economic Research at the Bedford VA. Assistant Professor, Boston University School of Medicine. Percent time in therapeutic INR range (TTR). 2010 Oct 7. 8 p.

## Measure Availability

The individual measure, "Percent Time in Therapeutic INR Range (TTR)," is available from the developer.

For more information, please contact Dr. Adam Rose at [adamrose@bu.edu](mailto:adamrose@bu.edu).

## Companion Documents

The following are available:

- Rose AJ, Hylek EM, Ozonoff A, Ash AS, Reisman JI, Berlowitz DR. Risk-adjusted percent time in therapeutic range as a quality indicator for outpatient oral anticoagulation: results of the Veterans Affairs Study To Improve Anticoagulation (VARIA). *Circ Cardiovasc Qual*

Outcomes 2011 Jan 1;4(1):22-29. This document is available from the [American Heart Association Web site](#) .

- Rose AJ, Hylek EM, Ozonoff A, Ash AS, Reisman JI, Berlowitz DR. Patient characteristics associated with oral anticoagulation control: results of the Veterans Affairs Study to Improve Anticoagulation (VARIA). *J Thromb Haemost* 2010 Oct;8(10):2182-91.

For more information, please contact Dr. Adam Rose at [adamrose@bu.edu](mailto:adamrose@bu.edu).

## NQMC Status

This NQMC summary was completed by ECRI Institute on April 14, 2011. The information was verified by the measure developer on April 21, 2011.

## Copyright Statement

This measure represents the work of the authors alone and does not necessarily represent the official views or policies of the Department of Veterans Affairs. For further information regarding this measure, contact Adam Rose at [adam.rose@va.gov](mailto:adam.rose@va.gov).

## Disclaimer

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