Venous Thrombosis Research Supported by NHLBI

Susan Shurin, M.D.

Deputy Director, NHLBI
Acting Division Director,
Division of Blood Diseases and Resources
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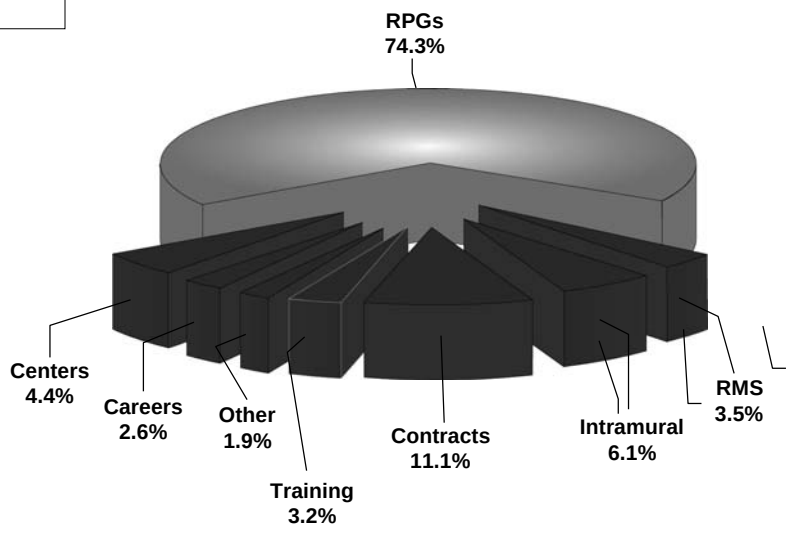
NHLBI Budget Mechanism FY 2009 President's Budget



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Division of Blood Diseases, Thrombosis and Hemostasis Branch

Research Interest :

•Functional and translational studies of coagulation, thrombolysis, and platelet biology

•Studies of risk factors, diagnosis, prevention and treatment for thrombotic and bleeding disorders

•Understanding the complex mechanisms that result in venous and arterial thrombosis

•Studies of genetic and immune induced bleeding disorders

•Investigations of the interplay of proteins, blood cells and vasculature on hemostasis and thrombosis

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Division of Cardiovascular Diseases Atherothrombosis/Coronary Artery Disease Branch

Focus is on arterial, not venous, thrombosis

- Initiation, progression, and regression of atherosclerotic lesions in arterial beds; lesion instability and thrombosis;
- Interaction of lipid fractions and other systemic and humoral factors with the arterial wall;
- Biomarker and imaging diagnostics
- Diet and exercise related to atherothrombosis.

Some of the research supported is relevant to DVT

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Examples of Investigator-Initiated Research in Venous Thrombosis, DBDR

- Genetic and acquired risk factors for venous thromboembolism
- Treatment and prophylaxis of the occult catheter-related DVT in pediatric population
- Oral contraception and hormone replacement therapy predisposition to venous thromboembolism
- Population-based surveillance for monitoring trends of DVT and pulmonary embolism
- Development of new integrated multifunctional imaging of deep venous thrombosis
- Clinical approaches to address DVT that minimize risk of post-thrombotic syndrome

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ATTRACT Trial

"Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis" (ATTRACT), Awarded - 2008

Collaboration between NHLBI and Venous Disease Coalition scientists to address the question of wide implementation of the Endovascular Thrombus Removal as first-line treatment of acute proximal DVT.

- 28 participating clinical centers
- 692 subjects planned for enrollment
- Dedicated data coordinating center and health economic core laboratory
- International (Canada) participation

Potential benefits: decreased incidence of post-thrombotic syndrome; patient's superior quality of life.

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Institute-Initiated Programs

- Related to Strategic Plan
- Requires NHLBI leadership
- Complements investigator initiated research
- Proposed program is
  - needed to stimulate scientific area
  - timely
  - reviewed by NHLBI staff, Board of External Experts, and NHLBI Advisory Council

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Institute-Initiated Programs Supporting Research on Venous Thrombosis

Initiative	No. Awards	Millions
Critical Issues in Post-Phlebitic Syndrome (FY 2006-2009)	3	$4.5
Venous Thrombosis and Thromboembolism in the Elderly (FY 2007-FY 2011) (NIA Lead IC)	8	$10.0 est.
Deep Vein Thrombosis and Venous Disease	6-8 est.	$25.0 est

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Critical Issues in Post-Phlebitic Syndrome

Goal of the Initiative: To support research on venous biology and post-thrombotic response of vein-wall and valve function.

Research areas:

- Phenotypic and genetic molecular biomarkers of post-thrombotic syndrome
- Role of matrixmetalloproteinases (MMP) proteins in thrombus resolution
- Mechanistic insight into the pathophysiology of post-phlebitic syndrome

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Venous Thrombosis and Thromboembolism in the Elderly

Goal of the Initiative: To improve the health and well-being of elderly patients at risk for thrombotic and thromboembolic events and improve understanding of factors that contribute to age related increase in thrombosis.

Research areas:

- Influence of age on the role of platelets in the pathogenesis of VTE
- Risk of heparin-induced thrombocytopenia in older patients
- Aging-associated pro-oxidative state on venous thrombosis

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Deep Vein Thrombosis and Venous Disease

Goal of the initiative: Explore the mechanisms of venous thromboembolism initiation, progression and recurrence and support clinical/translational studies to improve diagnosis and therapy.

Characteristics:

- Required clinical research component
- Collaborative studies and resource sharing
- Planned interactions with CDC Thrombosis and Hemostasis program

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Deep Vein Thrombosis and Venous Disease

Research areas:

- VTE prophylaxis in ambulatory cancer patients
- Safety and dosing of anticoagulation for children with thrombosis
- Clinical characteristics and biomarkers for VTE risk
- Progression and recurrence, and potential new therapeutic agents for VTE

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Improved therapies: we have a way to go

Existing therapies all have drawbacks and complications

- Require monitoring: More prescriptions are written for Warfarin^{R} each year than any other drug in the US
- Difficult to administer: Heparin, heparin variants
- Expensive: Antiplatelet agents

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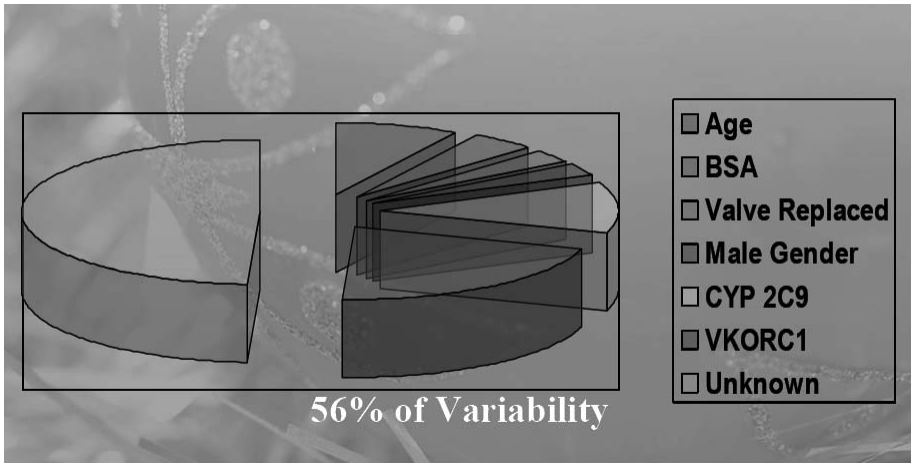
Factors Affecting Variability in Warfarin^{R} Dosing



From: Michael Caldwell

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Warfarin^{R} Dosing: ? Need for trial?

About 56% of the variance in warfarin dose is explained by a combination of clinical and genetic factors.

Use of this information is not known to improve clinical outcomes.

Both laboratory measures and clinical outcomes (bleeding/clotting) are important.

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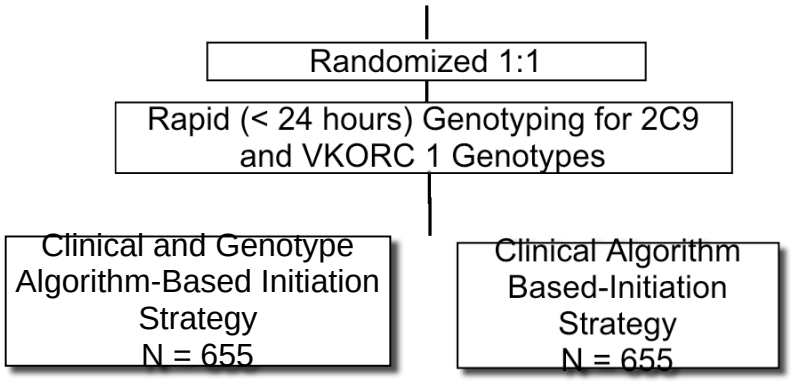
Randomized Trial of Genotype-Guided Dosing of Warfarin^{R} Therapy (COAG)

Eligibility: Patients with indication for > 3 months warfarin therapy
Exclude: Patients with contra-indication to warfarin therapy



Subsequent doses adjustments based on INR response

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Summary

NHLBI supports a robust portfolio of research on venous thromboembolism

Urgently needed:

- better diagnostics and therapeutics
- more prevention and awareness
- better implementation of the things we know

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Information from NHLBI for Researchers, Patients and the Public

NHLBI Public Website:
http://www.nhlbi.nih.gov/index.htm

DBDR Public Website:
http://www.nhlbi.nih.gov/about/dbdr/index.htm

Health information on blood diseases:
http://www.nhlbi.nih.gov/health/public/blood/index.htm

ClinicalTrials.gov:
http://clinicaltrials.gov/

DVT:
http://www.nhlbi.nih.gov/health/dci/Diseases/Dvt/DVT_WhatIs.html

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