SISET

XXIV CONGRESSO NAZIONALE
SISET
9-12 novembre 2016

Societa' Italiana per lo Studio
dell'Emostasi e della Trombosi

## Simposio SISET/SIPMEL/SIBIOC

***"Le sfide diagnostiche del laboratorio di coagulazione"***

Moderatori: M. Ciaccio (SIBIOC), A. Falanga (SISET), M. Golato (SIPMEL)

*Il laboratorio rispetto all' innovazione nell'ambito delle terapie anticoagulanti*

D. Giavarina

# Monitoraggio terapia con warfarin

| Variabilità della sensibilità al farmaco - FARMACOGENETICA | POCT vs LAB |
| --- | --- |
| • Polimorfismi citocromo P450 (2C9)<br>• Polimorfismi dell'enzima vitamina K epossido-reduttasi | • Laboratorio e Specialista<br>• Laboratorio e MMG<br>• Centri FCSA<br>• patient self-testing" (PST)<br>• patient self-management (PSM) |

# Anticoagulanti orali: Relazione dose risposta

## Fattori genetici

l'enzima 2C9 del citocromo P450 è responsabile del metabolismo ossidativo del S-isomero del warfarin.

I portatori delle varianti CYP2C9*2 (15%) e CYP2C9*3 (7%) hanno una significativa riduzione della velocità di eliminazione del S-enantiomero del warfarin e dell'acenocumarolo

L'omozigosi CYP2C9*3 ha un fabbisogno ridotto di circa il 25%

# Anticoagulanti orali: Relazione dose risposta

## Fattori genetici

Numerose varianti del gene codificante per l'enzima Vitamina K-epossido riduttasi (VKORC1) determinano una diversa sensibilità al warfarin.

L'aplotipo VKORC1*2 è responsabile di una riduzione dei livelli trascrizionali dell'enzima del 30-50% (Rieder MJ et al. N Engl J Med 2005).

Marcata segregazione etnica per VKORC1*2:

| | |
|---|---|
| Asiatici | 95%; |
| Africani | 15% |
| Caucasici | 40% |

# Anticoagulanti orali: Relazione dose risposta

## Fattori genetici

Essere portatori contemporaneamente del polimorfismo CYP2C9 e VKORC1 è associato con un elevato rischio di sviluppare episodi di iperdosaggio in corso di trattamento con dicumarolici (OR 3.8)

(Schalekamp T et al. 2006)

# Estimation of the Warfarin Dose with Clinical and Pharmacogenetic Data

The International Warfarin Pharmacogenetics Consortium*

New England J Med,2009

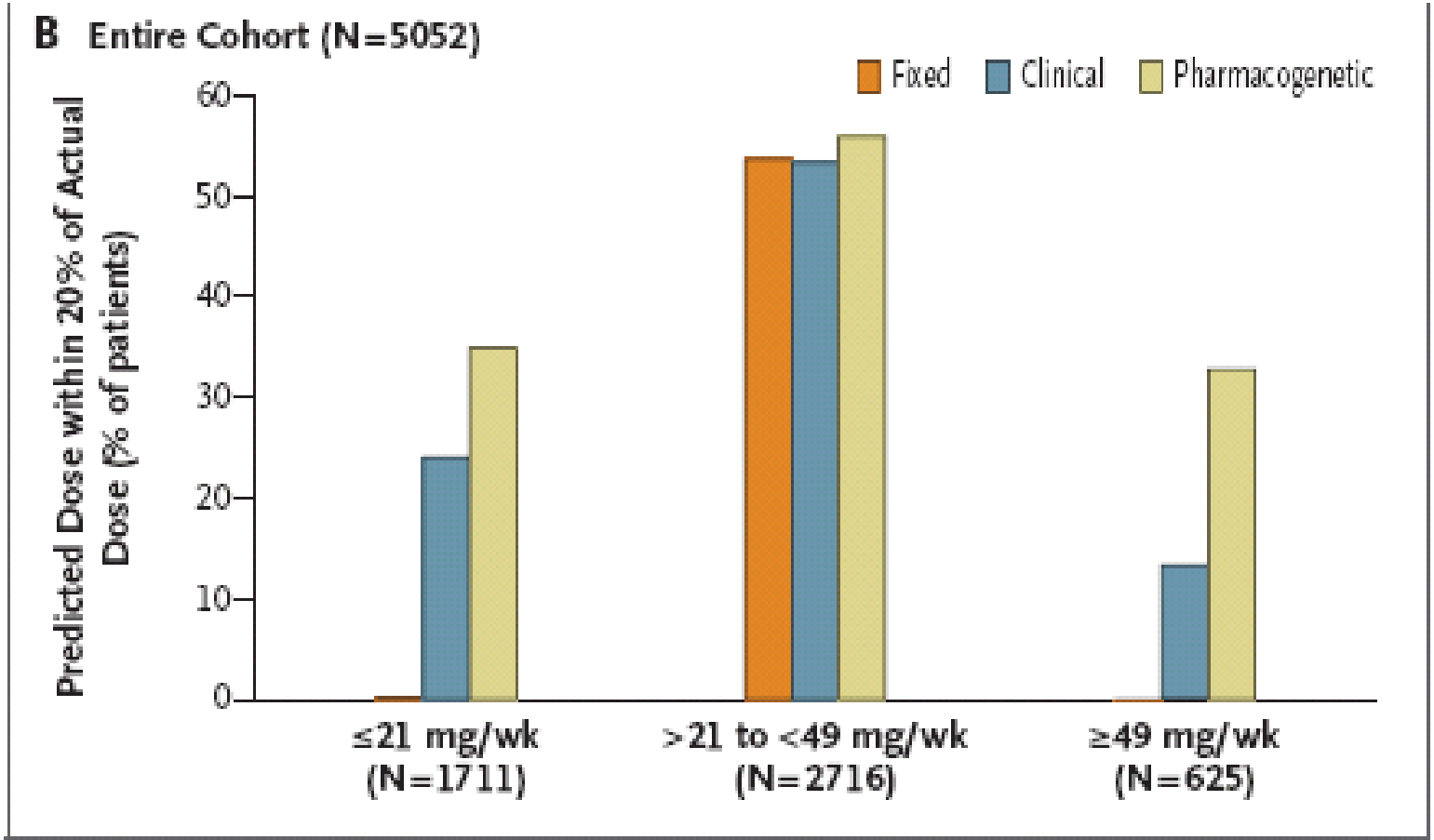



**Figure 2.** Percentage of Patients with Dose Estimates within 20% of the Actual Dose, as Derived with the Use of a Pharmacogenetic Algorithm, a Clinical Algorithm, and a Fixed-Dose Approach.

# Genotype-Guided vs Clinical Dosing of Warfarin and Its Analogues

## Meta-analysis of Randomized Clinical Trials

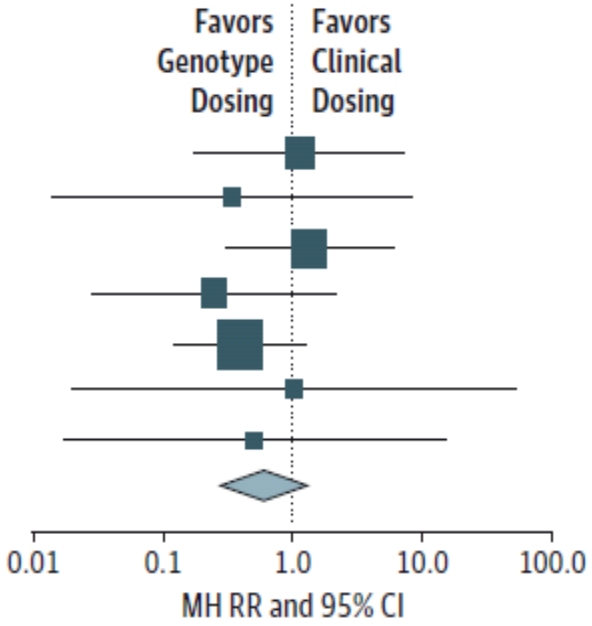
Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

JAMA, 2014

Thromboembolic events

C

| Source | RR | Lower Limit | Upper Limit | z Score Value | P Value |
|---|---|---|---|---|---|
| Hillman et al,[27] 2005 | 1.11 | 0.17 | 7.09 | 0.11 | .91 |
| Caraco et al,[29] 2008 | 0.34 | 0.01 | 8.17 | -0.67 | .50 |
| Burmester et al,[30] 2011 | 1.33 | 0.31 | 5.82 | 0.38 | .70 |
| Jonas et al,[32] 2013 | 0.25 | 0.03 | 2.13 | -1.28 | .20 |
| Kimmel et al,[33] 2013 | 0.39 | 0.12 | 1.24 | -1.60 | .11 |
| Primohamed et al,[34] 2013 | 1.00 | 0.02 | 50.40 | 0.00 | >.99 |
| Verhoef et al,[35] 2013 | 0.50 | 0.02 | 14.95 | -0.40 | .69 |
| Overall | 0.60 | 0.29 | 1.22 | -1.42 | .16 |



# Genotype-Guided vs Clinical Dosing of Warfarin and Its Analogues

## Meta-analysis of Randomized Clinical Trials

Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

JAMA, 2014

Bleedings

C

| Source | RR | Lower Limit | Upper Limit |
|---|---|---|---|
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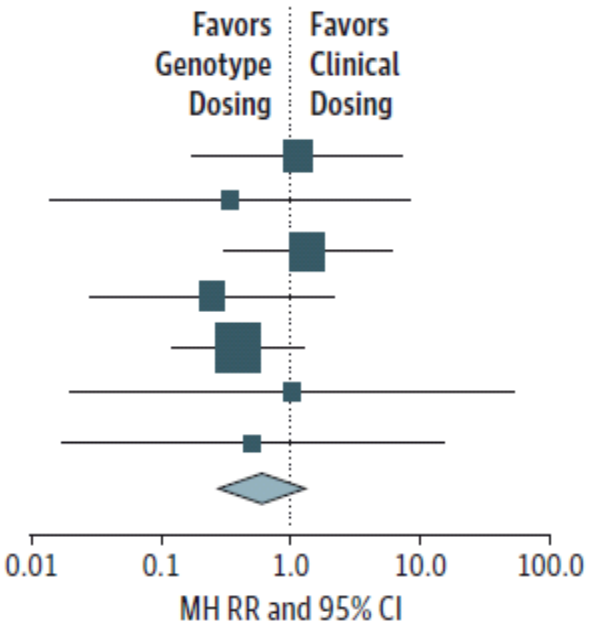


# ACCP Guidelines Antithrombotic and Thrombolitic therapy

**9th Edition; CHEST 2012**
**Holbrook A et al.**

**2.2. For patients initiating VKA therapy, we recommend against the routine use of pharmacogenetic testing for guiding doses of VKA** (Grade 1B) **.**

# A Simple Scheme to Initiate Oral Anticoagulant Treatment in Outpatients With Nonrheumatic Atrial Fibrillation

Vittorio Pengo, MD, Alessandra Biasiolo, DSci, and Cinzia Pegoraro, MD

**TABLE 1** Predicted Weekly Warfarin Maintenance Dose on the Basis of INR on Day 5 After 5 mg/day of Warfarin for Four Consecutive Days*

| INR on Day 5 | mg/wk |
|---|---|
| 1.0 | 71 |
| 1.1 | 57 |
| 1.2 | 48 |
| 1.3 | 43 |
| 1.4 | 39 |
| 1.5 | 35 |
| 1.6 | 33 |
| 1.7 | 31 |
| 1.8 | 29 |
| 1.9 | 27 |
| 2.0 | 26 |
| 2.1 | 24 |
| 2.2 | 23 |
| 2.3 | 22 |
| 2.4 | 21 |
| 2.5 | 20 |
| 3.0 | 16 |

| INR 5° giorno | Warfarin mg/sett |
|---|---|
| 3.4 | 13 |
| 3.9 | 10 |
| 4.3 | 7.5 |

Am J Cardiol, 2001

# POCT: from 1969 to today

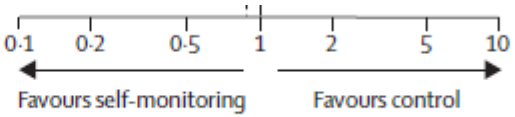
Self-monitoring of oral anticoagulation: systematic review and meta-analysis of individual patient data

Carl Heneghan, Alison Ward, Rafael Perera, and The Self-Monitoring Trialist Collaboration

Lancet 2012; 379: 322–34

# Anticoagulanti orali: POCT vs Laboratorio

| A | Self-monitoring | Control | O-E | Variance | Hazard ratio (random) | HR (95% CI) | Interaction test |
|---|---|---|---|---|---|---|---|
| **Sex** | | | | | | | |
| Male | 96/2453 | 124/2323 | −17·57 | 54·73 | | 0·40 (0·20–0·80) | |
| Female | 18/539 | 28/555 | −3·28 | 11·13 | | 0·76 (0·36–1·58) | p=0·94 |
| **Age (years)** | | | | | | | |
| <55 | 11/496 | 25/338 | −9·17 | 8·37 | | 0·33 (0·17–0·66) | |
| 55–64 | 33/895 | 34/798 | −2·17 | 16·59 | | 0·80 (0·45–1·42) | |
| 65–74 | 44/1038 | 66/1117 | −9·88 | 27·06 | | 0·69 (0·48–1·01) | |
| ≥75 | 26/488 | 27/538 | 1·02 | 13·03 | | 0·96 (0·41–2·26) | p=0·052 |
| **Indication** | | | | | | | |
| Mechanical valve | 36/1132 | 63/1040 | −16·22 | 24·58 | | 0·52 (0·35–0·77) | |
| Atrial fibrillation | 70/1629 | 69/1623 | −0·06 | 34·58 | | 0·67 (0·28–1·57) | |
| Other | 8/261 | 20/237 | −3·87 | 6·30 | | 0·54 (0·25–1·18) | p=0·032 |
| **Self-monitoring** | | | | | | | |
| Self-testing only | 89/1566 | 89/1557 | −2·83 | 44·44 | | 0·74 (0·30–1·82) | |
| Self-management | 25/1487 | 63/1382 | −18·52 | 21·57 | | 0·42 (0·28–0·65) | p=0·002 |
| **Type of control group care** | | | | | | | |
| Anticoagulation clinic | 92/1959 | 112/1950 | −11·46 | 50·83 | | 0·44 (0·17–1·14) | |
| Primary care | 16/995 | 27/893 | −6·34 | 10·44 | | 0·55 (0·28–1·08) | p=0·34 |
| **Total** | **114/3053** | **152/2939** | | | | **0·51 (0·31–0·85)** | |




Thrombosis (A)

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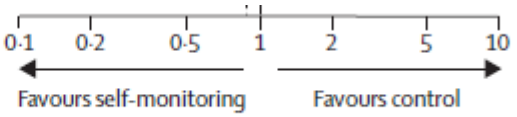
Carl Heneghan, Alison Ward, Rafael Perera, and The Self-Monitoring Trialist Collaboration

Lancet 2012; 379: 322–34

# Anticoagulanti orali: POCT vs Laboratorio

| B | Self-monitoring | Control | O–E | Variance | Hazard ratio (random) | HR (95% CI) | Interaction test |
|---|---|---|---|---|---|---|---|
| **Sex** | | | | | | | |
| Male | 201/2542 | 201/2403 | −9·86 | 99·83 | | 0·91 (0·74–1·10) | |
| Female | 29/618 | 43/639 | −5·15 | 17·56 | | 0·75 (0·47–1·19) | p=0·45 |
| **Age (years)** | | | | | | | |
| <55 | 25/500 | 24/340 | −2·71 | 11·79 | | 0·79 (0·45–1·41) | |
| 55–64 | 66/812 | 44/699 | 6·67 | 27·16 | | 1·28 (0·88–1·86) | |
| 65–74 | 78/1110 | 101/1185 | −11·66 | 43·86 | | 0·77 (0·57–1·03) | |
| ≥75 | 61/583 | 75/640 | −4·48 | 33·49 | | 0·87 (0·62–1·23) | p=0·20 |
| **Indication** | | | | | | | |
| Mechanical valve | 78/1111 | 91/1015 | −10·11 | 41·66 | | 0·78 (0·58–1·06) | |
| Atrial fibrillation | 126/1676 | 119/1677 | 2·35 | 60·60 | | 1·04 (0·81–1·34) | |
| Other | 26/260 | 34/281 | −6·90 | 13·87 | | 0·61 (0·36–1·03) | p=0·13 |
| **Self-monitoring** | | | | | | | |
| Self-testing only | 190/1729 | 200/1719 | −11·41 | 96·81 | | 0·84 (0·64–1·12) | |
| Self-management | 40/1487 | 44/1382 | −3·27 | 20·89 | | 0·86 (0·56–1·31) | p=0·87 |
| **Type of control group care** | | | | | | | |
| Anticoagulation clinic | 182/1959 | 187/1950 | −8·27 | 91·58 | | 0·91 (0·74–1·12) | |
| Primary care | 42/1158 | 46/1055 | −4·02 | 21·89 | | 0·83 (0·50–1·36) | p=0·60 |
| **Total** | **230/3216** | **244/3101** | | | | **0·88 (0·74–1·06)** | |




major haemorrhage (B)

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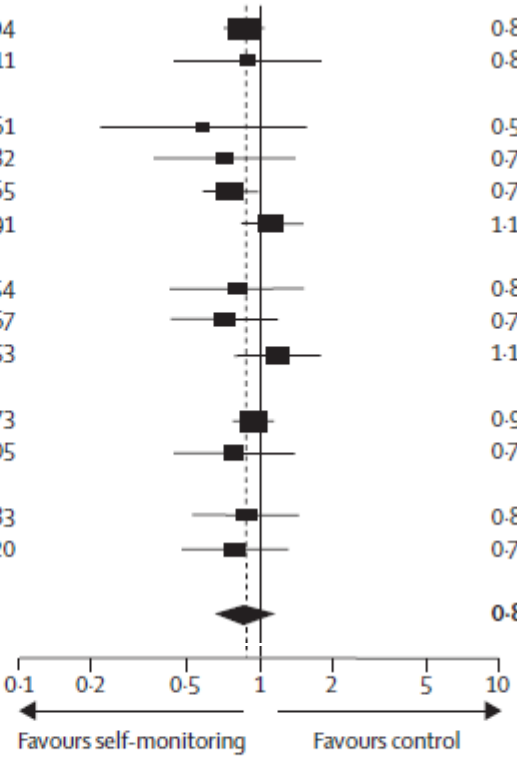
Lancet 2012; 379: 322–34

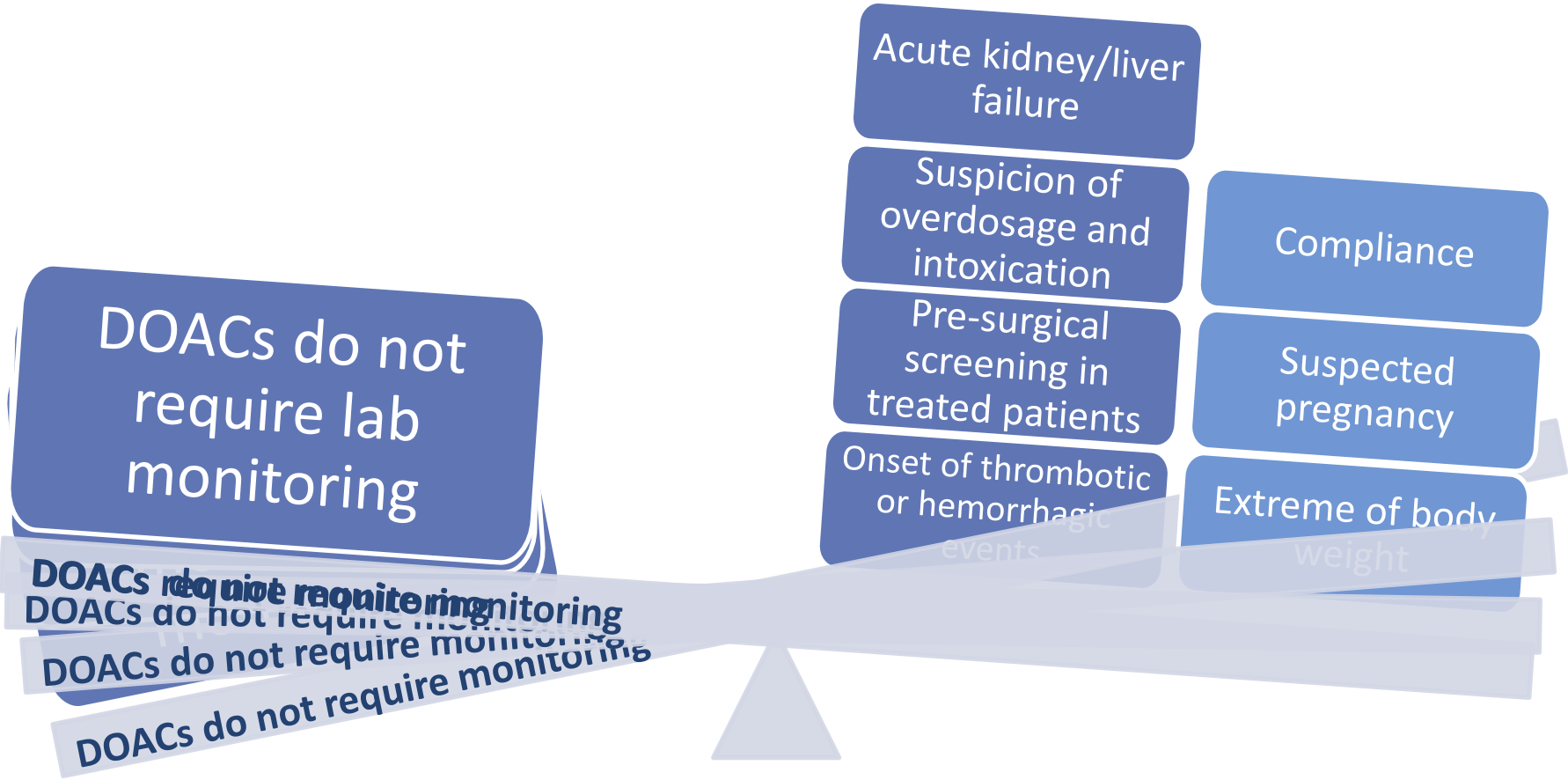
# Anticoagulanti orali: POCT vs Laboratorio

| C | Self-monitoring | Control | O–E | Variance | Hazard ratio (random) | HR (95% CI) | Interaction test |
|---|---|---|---|---|---|---|---|
| **Sex** | | | | | | | |
| Male | 204/2440 | 219/2297 | −17·06 | 105·04 | | 0·85 (0·70–1·03) | |
| Female | 43/618 | 55/639 | −2·81 | 24·11 | | 0·89 (0·44–1·81) | p=0·84 |
| **Age (years)** | | | | | | | |
| <55 | 14/495 | 15/353 | −3·56 | 6·61 | | 0·58 (0·22–1·57) | |
| 55–64 | 46/874 | 46/781 | −2·84 | 22·82 | | 0·72 (0·36–1·41) | |
| 65–74 | 98/1034 | 129/1112 | −15·44 | 55·65 | | 0·76 (0·58–0·99) | |
| ≥75 | 89/583 | 84/640 | 4·74 | 42·91 | | 1·12 (0·83–1·51) | p=0·19 |
| **Indication** | | | | | | | |
| Mechanical valve | 64/1101 | 75/1002 | −9·66 | 34·54 | | 0·80 (0·42–1·52) | |
| Atrial fibrillation | 138/1555 | 156/1549 | −14·32 | 72·67 | | 0·72 (0·43–1·20) | |
| Other | 45/334 | 43/349 | 3·71 | 21·53 | | 1·19 (0·78–1·81) | p=0·23 |
| **Self-monitoring** | | | | | | | |
| Self-testing only | 195/1729 | 201/1719 | −8·94 | 98·73 | | 0·91 (0·75–1·11) | |
| Self-management | 52/1342 | 73/1237 | −12·04 | 31·05 | | 0·75 (0·42–1·33) | p=0·15 |
| **Type of control group care** | | | | | | | |
| Anticoagulation clinic | 159/1934 | 173/1926 | −10·62 | 82·83 | | 0·82 (0·52–1·28) | |
| Primary care | 72/988 | 90/884 | −13·02 | 40·20 | | 0·72 (0·44–1·18) | p=0·20 |
| **Total** | **247/3071** | **274/2956** | | | | **0·82 (0·62–1·09)** | |




death (C).

# DOACS


DOACs do not require lab monitoring
Acute kidney/liver failure
Suspicion of overdosage and intoxication
Pre-surgical screening in treated patients
Onset of thrombotic or hemorrhagic events
Compliance
Suspected pregnancy
Extreme of body weight

# DOACS e Laboratorio: quesiti

| | |
|---|---|
| **Esami** | • Screening Coagulativi?<br>• Monitoraggio terapeutico del farmaco? |
| **Tempi** | • Routine<br>• Urgenza |
| **Interpretazione** | • Referto<br>  • Valori decisionali, Commenti, … |

# LA LOGICA DIAGNOSTICA 1988

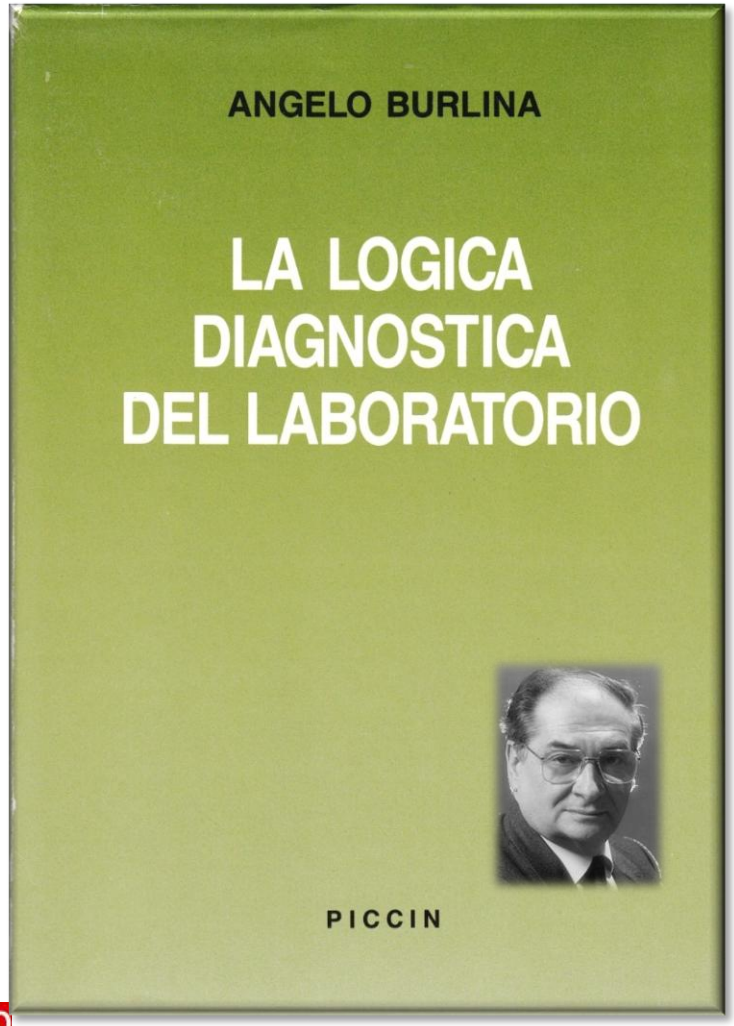
- **Finalizzata esclusivamente ai problemi decisionali del clinico**

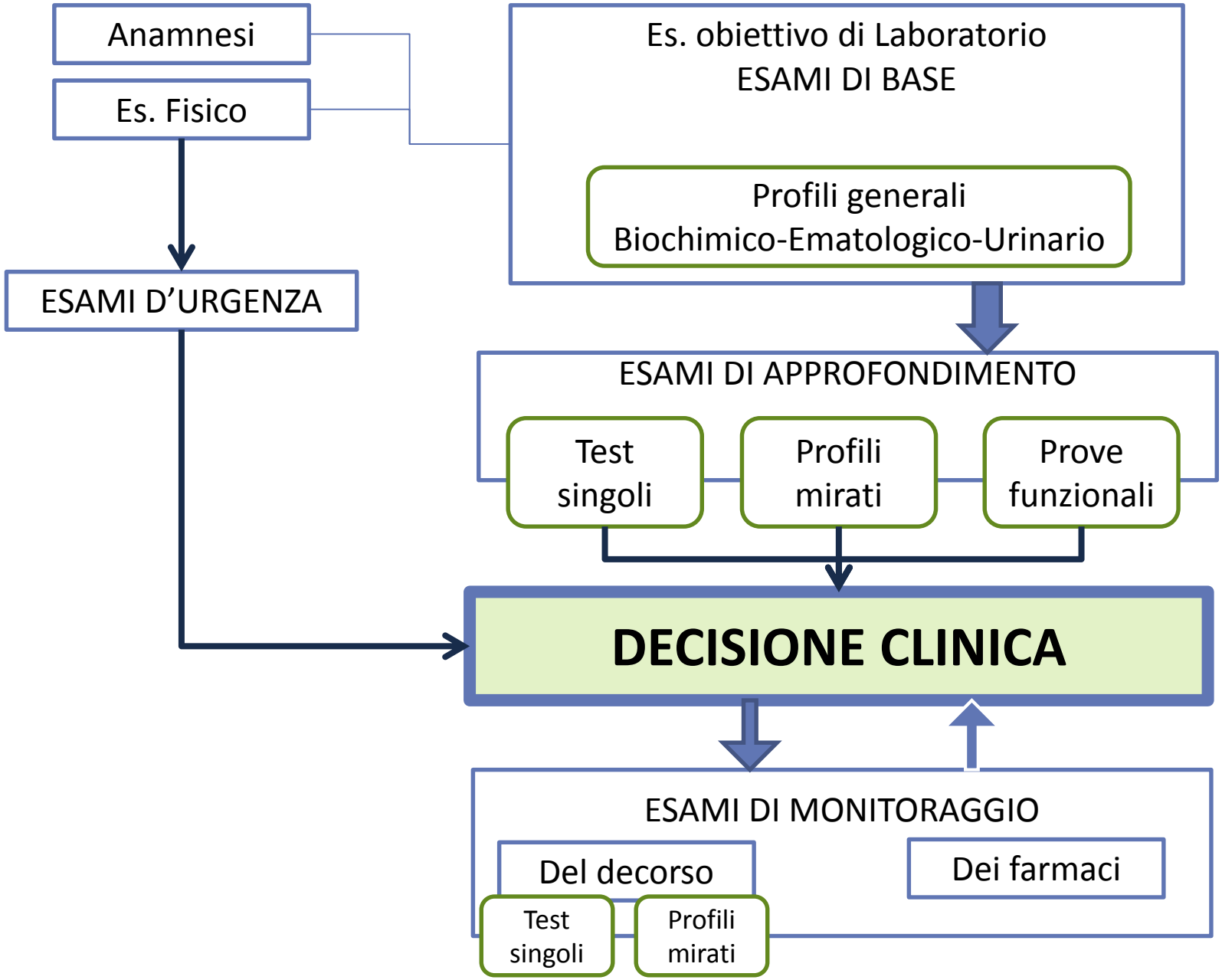
Esami d'urgenza

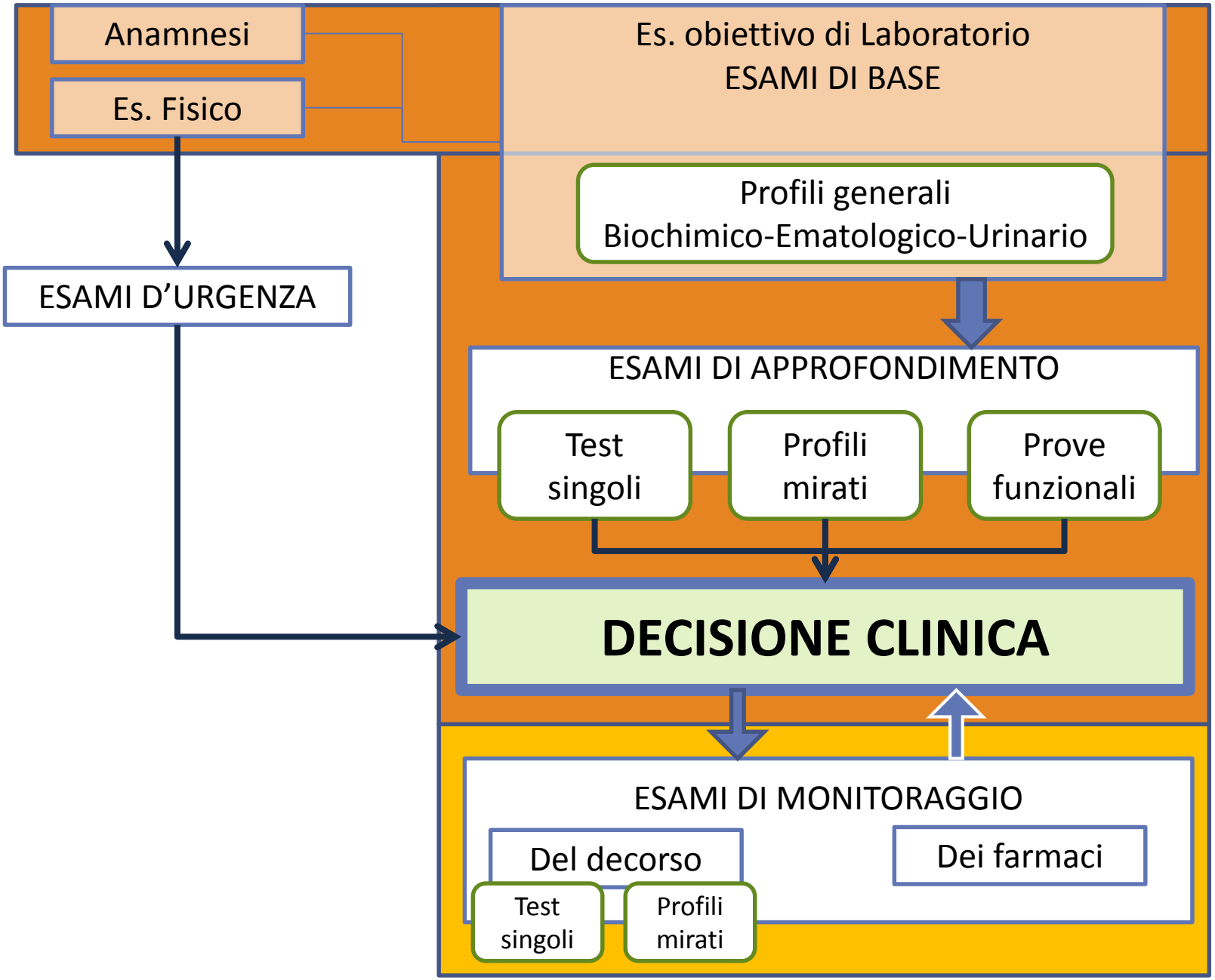
Esami diagnostici

- di base
  (l'esame obiettivo di laboratorio)
- di approfondimento

Esami di monitoraggio




Anamnesi
Es. Fisico
Es. obiettivo di Laboratorio
ESAMI DI BASE
Profili generali
Biochimico-Ematologico-Urinario
ESAMI D'URGENZA
ESAMI DI APPROFONDIMENTO
Test singoli
Profili mirati
Prove funzionali
DECISIONE CLINICA
ESAMI DI MONITORAGGIO
Del decorso
Test singoli
Profili mirati
Dei farmaci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DECISIONE CLINICA
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Del decorso
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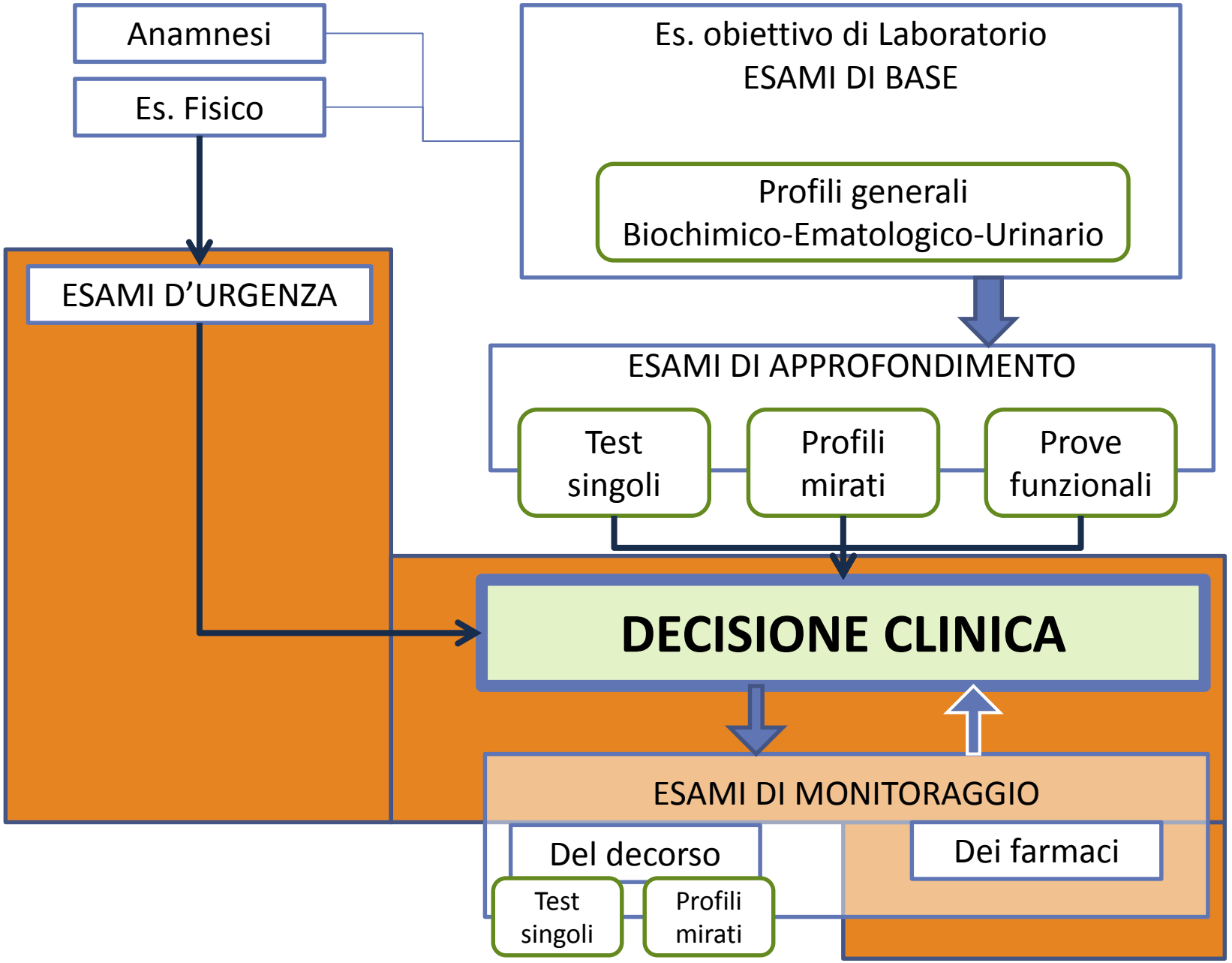
Profili mirati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Test singoli
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Prove funzionali
DECISIONE CLINICA
ESAMI DI MONITORAGGIO
Del decorso
Test singoli
Profili mirati
Dei farmaci

# XXI secolo

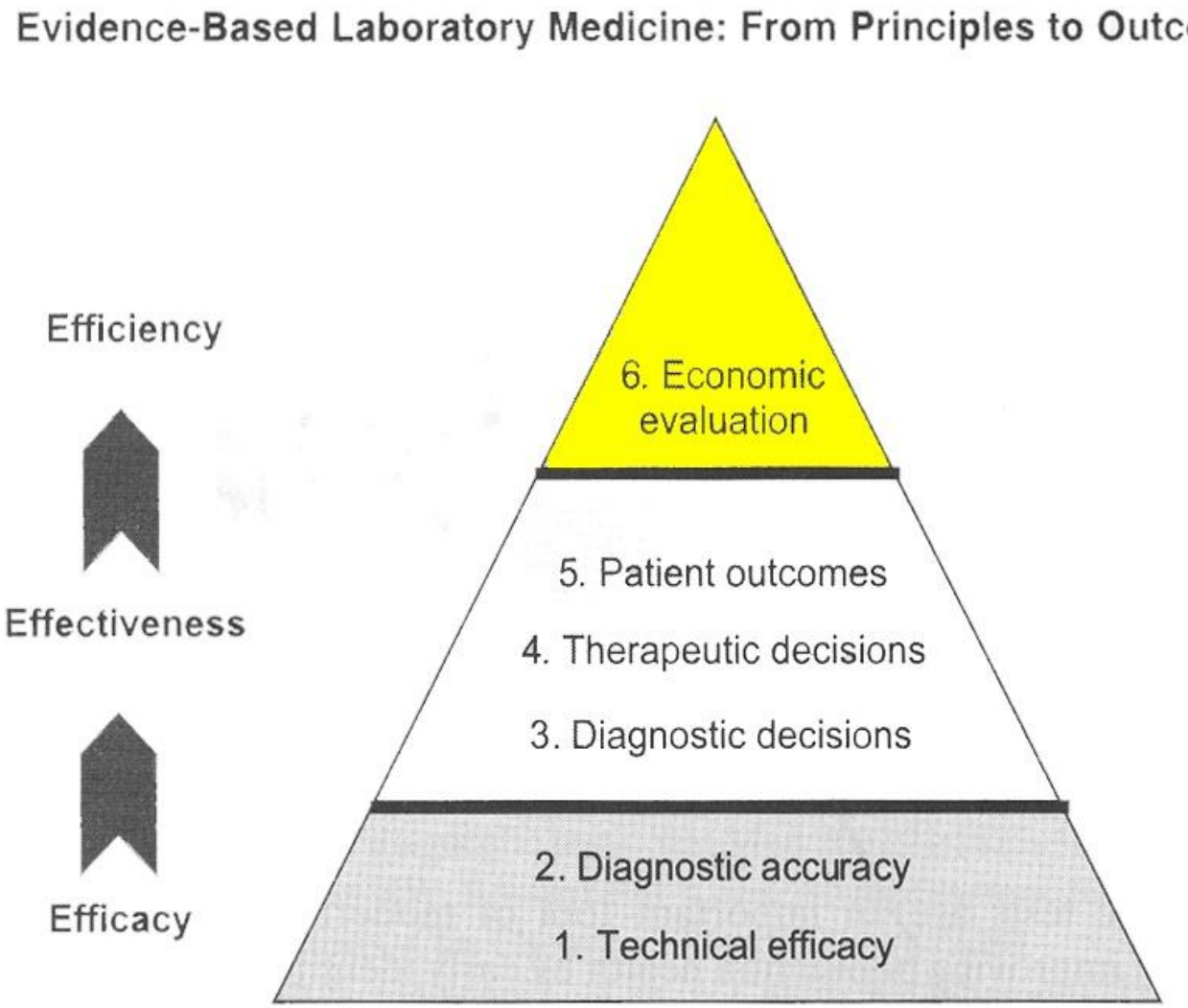


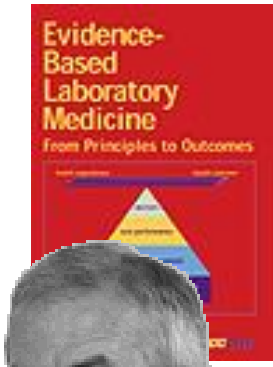

PAZIENTE

DOMANDA → TEST → DECISIONE → AZIONE

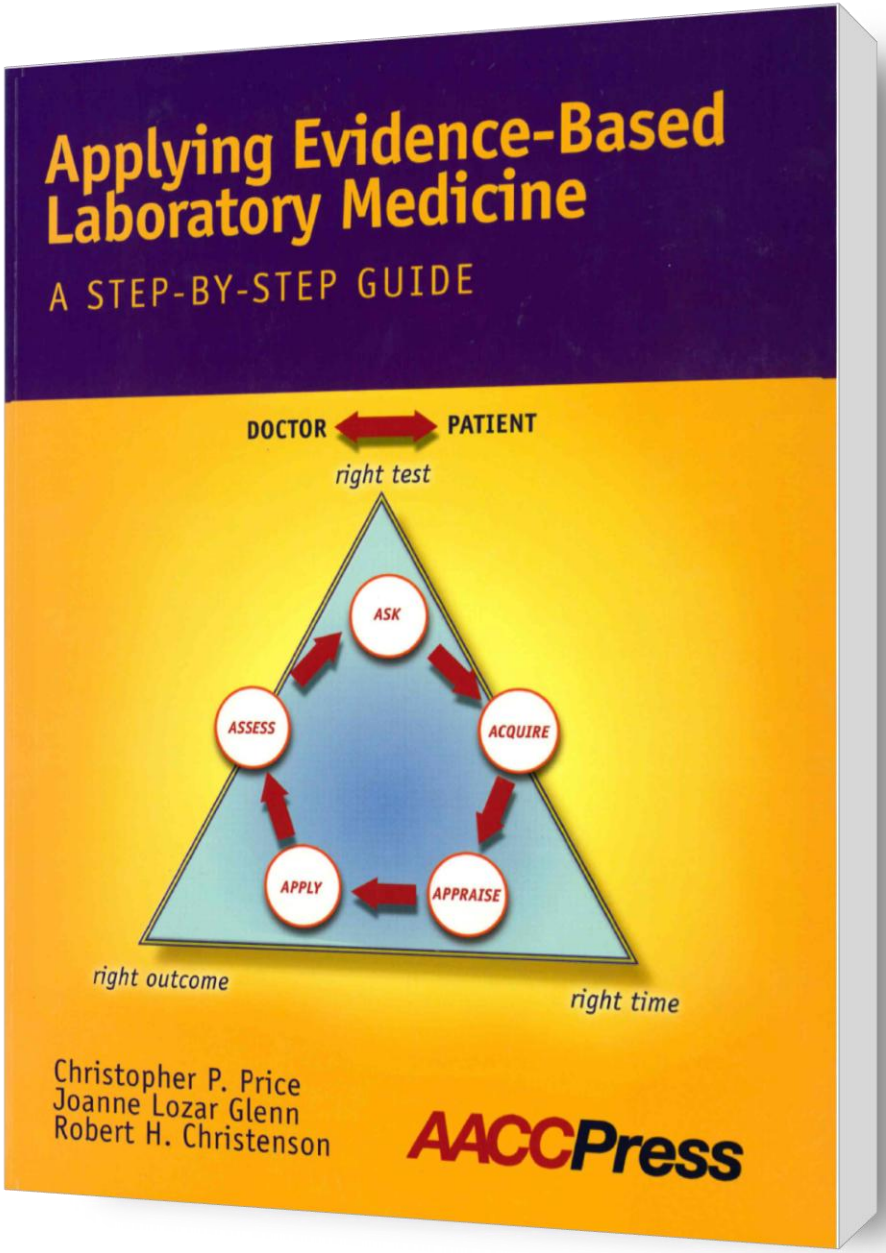
OUTCOME

# LA PIRAMIDE DELLA SCELTA IN LABORATORIO




C. Price


Applying Evidence-Based Laboratory Medicine
A STEP-BY-STEP GUIDE
DOCTOR
PATIENT
right test
ASK
ACQUIRE
APPRAISE
APPLY
ASSESS
right outcome
right time
Christopher P. Price
Joanne Lozar Glenn
Robert H. Christenson
AACCPress

# Il ciclo A5 per praticare l'EBLM


- Formulare la DOMANDA che descriva il problema
- Domanda cui sia possibile rispondere

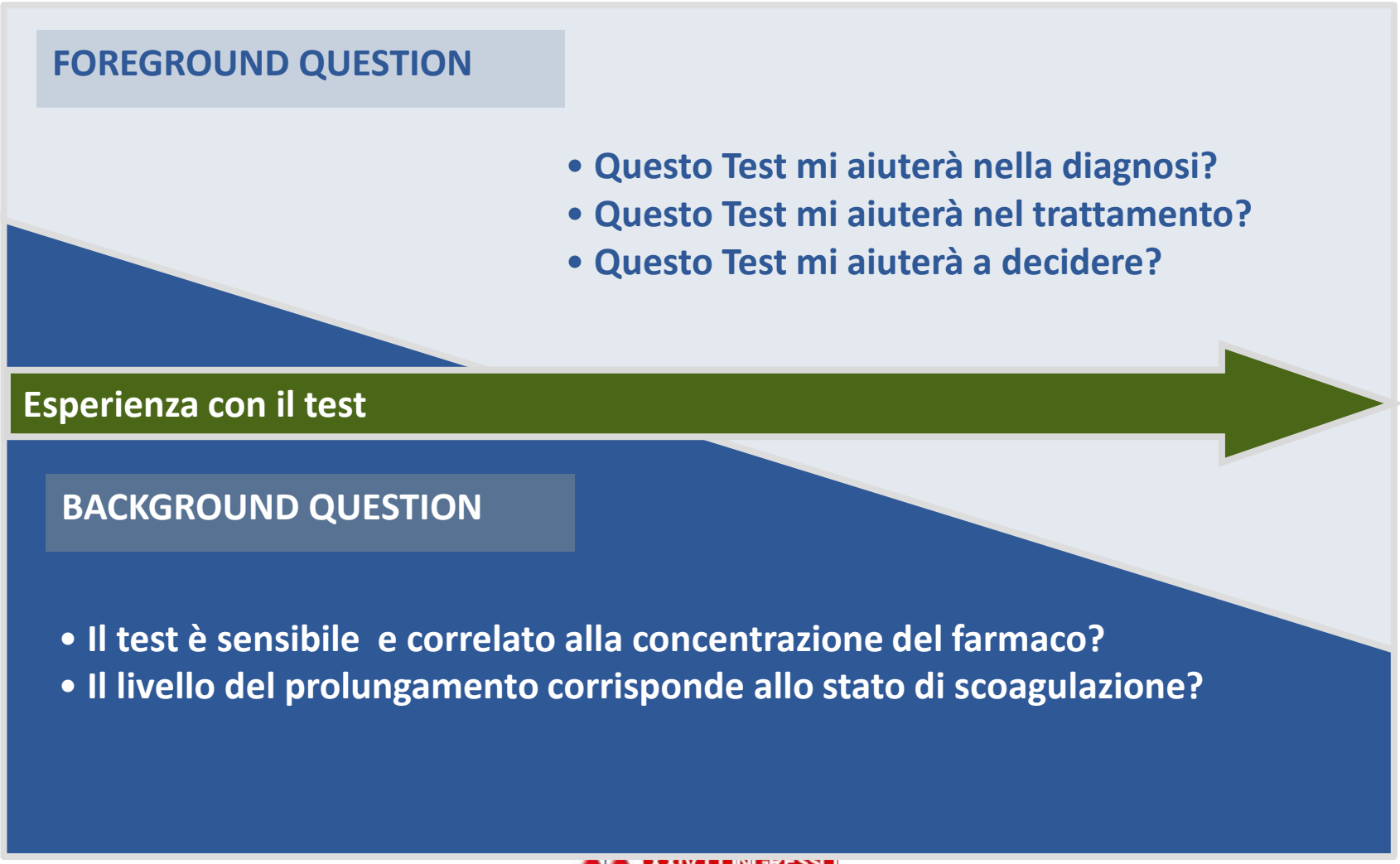
- Trovare le prove di efficacia (evidence) sul quesito

- Valutare le evidenza per rilevanza e qualità

- Applicare la conoscenza che è derivata dai passi precedenti per risolvere il problema

- Valutare con processi di audit l'applicazione del test o della soluzione proposta per la conferma delle conoscenze e del processo di applicazione

# Background & Foreground question



# Il ciclo A5 per praticare l'EBLM


- Formulare la DOMANDA che descriva il problema
- Domanda cui sia possibile rispondere

- Trovare le prove di efficacia (evidence) sul quesito

- Valutare le evidenza per rilevanza e qualità

- Applicare la conoscenza che è derivata dai passi precedenti per risolvere il problema

- Valutare con processi di audit l'applicazione del test o della soluzione proposta per la conferma delle conoscenze e del processo di applicazione

# Questions and answers on the use of dabigatran and perpectives on the use of other new oral anticoagulants in patients with atrial fibrillation

## A consensus document of the Italian Federa

Vittorio Pengo[1]; Luciano Crippa[2]; Anna Falanga[3]; Guido Finazz
Sophie Testa[8]; Eros Tiraferri[9]; Alberto Tosetto[10]; Armando Tripc
[1]Clinical Cardiology, Thrombosis Centre, University of Padova, Padova, Italy; [2]Thromb
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INTERNAL MEDICINE JOURNAL

Internal Medicine Journal 44 (2014)

CLINICAL PERSPECTIVES

# New oral anticoagulants: a practical guide on prescription, laboratory testing and peri-procedural/bleedin management

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tock[8]

[1]Haemostasis Thrombosis Unit, The Alfred Hospital, [6]Haematology Department, Melbourne University, Department, St Vincent's Hospital, [4]Haemophilia Treatment Centre, SA Pathology, Royal Adelaide Hos Department, Concord Hospital, Sydney, New South Wales, [7]Pathology Queensland, Princess Alexan [3]Clinical Haematology, [8]Obstetric Medicine, National Women's Health, Auckland City Hospital, Auc

**Key words**
new oral anticoagulant, pharmacology, laboratory testing, perioperative management, bleeding.

**Correspondence**
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Email: Huyen.tran@monash.edu

**Abstract**

New oral anticoagulants (NOAC)
prevent systemic embolism in p
treatment and prevention of v
their pharmacology is invalua
of patients receiving these
occur, or the patient requi
and Haemostasis has set o
on current available ev
groups to receive NOA
stances and (iii) man
strategies to manag

# Hypercoagulable states: an algorithmic approach to laboratory testing and update on monitoring of direct oral anticoagulants

Megan O. Nak
eland, OH, United States

an result from a variety of inherited and, more commonly, acquire
the underlying cause of thrombosis in a patient is complicated bo
riety of clinical conditions that can cause hypercoagulability as w
al assay interferences. Using an algorithmic approach to hype
rovides the ability to tailor assay selection to the clinical scenari
mber of unnecessary tests performed, saving cost and time, a
lse results. New oral anticoagulants are powerful tools for mana
atients; however, their use introduces new challenges in terms
therapeutic monitoring. The coagulation laboratory plays an ess
nd treating hypercoagulable states. The input of laboratory p
to guide appropriate testing and synthesize interpretation

ic approach, Antiphospholipid syndrom
mboembolism

Clin Chem Lab Med 2015; 53(2): 18

DE GRUYTER

Opinion Paper

Giuseppe Lippi* and Emmanuel J. Favaloro

# Recent guidelines and recommendations for laboratory assessment of the direct oral anticoagulants (DOACs): is there consensus?

DOI 10.1515/cclm-2014-0767
Received July 25, 2014; accepted August 22, 2014; previously published online September 22, 2014

**Abstract:** A new generation of antithrombotic agents, which are conventionally known as direct oral anticoagulants (DOACs), have recently emerged and are
to be developed. These provide direct
thrombin (factor IIa; FIIa)
currently include
oxaban

recommendation, and instead there was generalized
port for direct quantitative assessment
assays and specific apixaban
ficient data for other
guidance

INTERNAL MEDICINE JOURNAL

*Internal Medicine Journal* **44** (2014)

CLINICAL PERSPECTIVES

# New oral anticoagulants: a practical guide on prescription, laboratory testing and peri-procedural/bleeding management

H. Tran,[1] J. Joseph,[2] L. Young,[3] S. McRae,[4] J. Curnow,[5] H. Nandurkar,[6] P. Wood[7] and C. McLintock[8]

## Methods

Experts in thromboembolic disorders representing the Australasian Society of Thrombosis and Haemostasis (ASTH) were invited to join the panel of guideline development. The process included reviewing up-to-date evidence and existing high-quality evidence-based international guidelines for NOAC. We conducted monthly teleconferences from 6 June 2012 to 19 June 2013 during which specific questions, drafting and revisions of the guideline were discussed. Further revisions were made by consensus through email. All eight members of the panel are the authors of this article.

Consensus recommendations were reached in an equitable manner. Agreement of all members of the expert panel was required in order to proceed with making the recommendation. We acknowledge the lack of evidence in this area and that the recommendations are based largely on expert opinions.

largely on expert opinions.

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http://dx.doi.org/10.1016/j.jacc.2014.05.065

# Laboratory Measurement of the Anticoagulant Activity of the Non–Vitamin K Oral Anticoagulants

Adam Cuker, MD, MS,* Deborah M. Siegal, MD, MSc,† Mark A. Crowther, MD, MSc,† David A. Garcia, MD‡

**CONCLUSIONS**

these effects facil
between drug lev
College of Cardiol

More information on the relationship between drug levels and clinical outcomes is needed.

The Author(s) *Thrombosis Journal* 2016, **14**(Suppl 1):17
DOI 10.1186/s12959-016-0111-3

Thrombosis Journal

REVIEW Open Access

# DOACs – advances and limitations in real world

Lai Heng Lee

*From* The 9th Congress of the Asian-Pacific Society on Thrombosis and Hemostasis
Taipei, Taiwan. 6-9 October 2016

## CONCLUSION

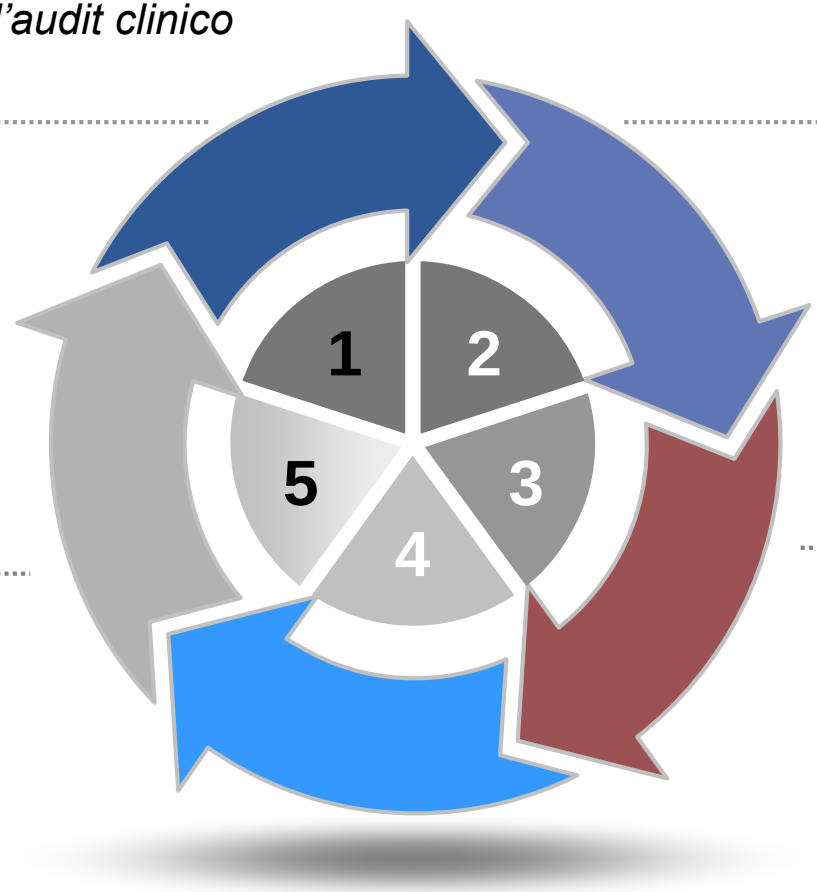
- DOACs represent an important advancement in antithrombotic management.
- Real world data consistent with their clinical trial data is reassuring

# Il miglioramento della Qualità nel Ciclo dell'Audit

*J.Barth ,2005, Il ruolo dell'audit clinico*

Cosa dovresti fare?

Cosa stai facendo?




C'è un miglioramento?

Perchè non stai facendo quello che dovresti fare?

Cosa avresti dovuto fare per migliorare?

*Journal of Thrombosis and Haemostasis*, **14**: 1–8 DOI: 10.1111/jth.13486

Final decision: F. R. Rosendaal, 19 August 2016

**ORIGINAL ARTICLE**

# Poor comparability of coagulation screening test with specific measurement in patients receiving direct oral anticoagulants: results from a multicenter/multiplatform study

S. TESTA,* C. LEGNANI,† A. TRIPODI,‡ O. PAOLETTI,* V. PENGO,§ R. ABBATE,¶ L. BASSI,* P. CARRARO,** M. CINI,† R. PANICCIA,¶ D. POLI¶ and G. PALARETI††

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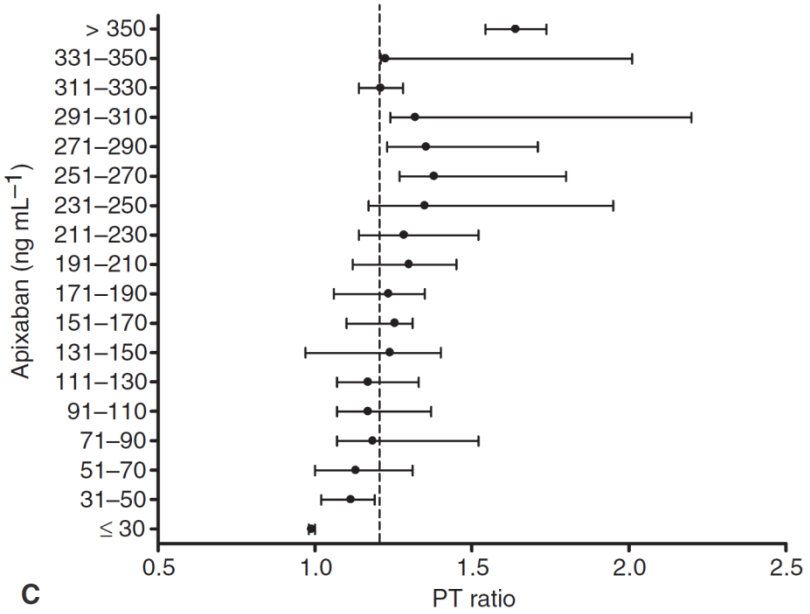
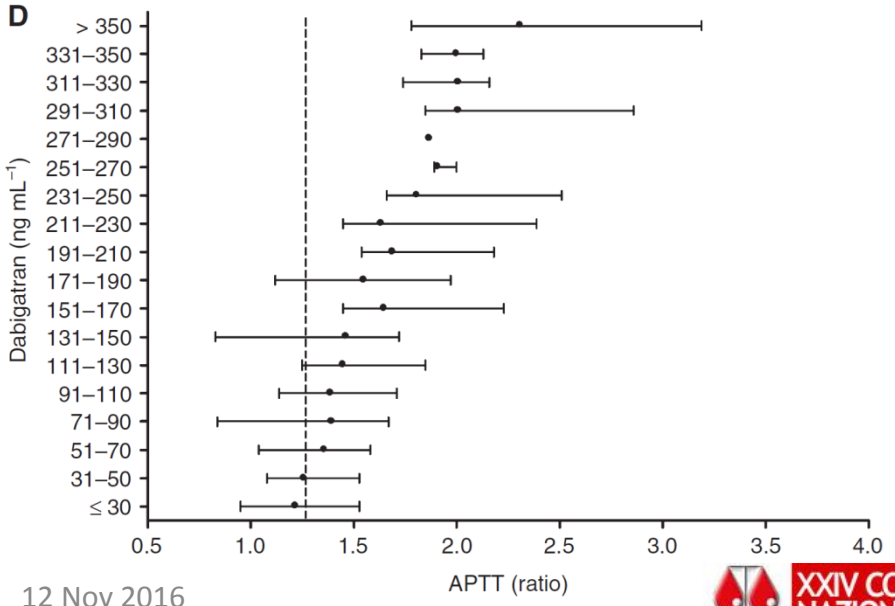
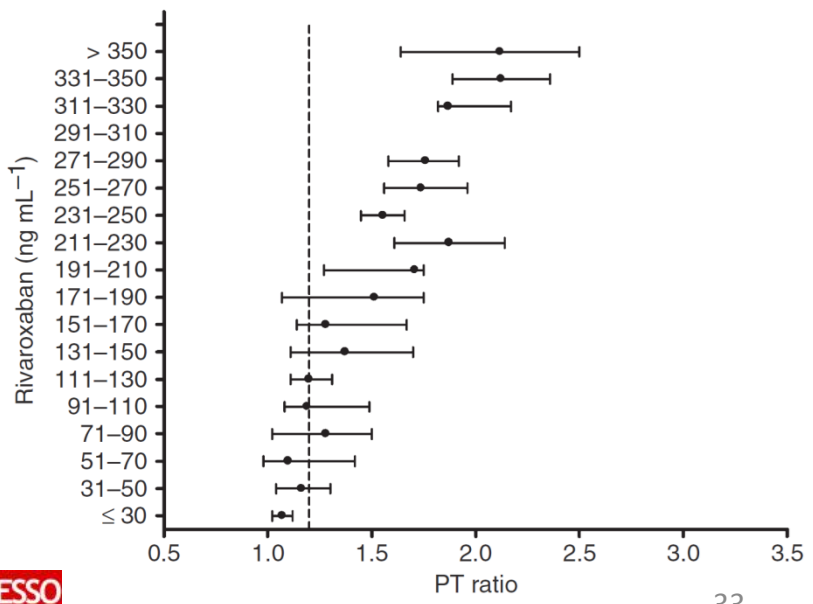


*Journal of Thrombosis and Haemostasis*, **14**: 1325–1327 DOI: 10.1111/jth.13344

FORUM

# To measure or not to measure direct oral anticoagulants before surgery or invasive procedures

A. TRIPODI

*Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Department of Clinical Sciences and Community Health, Università degli Studi di Milano and IRCCS Cà Granda Maggiore Hospital Foundation, Milan, Italy*

**Pharmacokinetic-strategy** | **Laboratory strategy**

- Overall, the laboratory strategy appears superior in terms of patient safety and should be considered in patients undergoing surgical or invasive procedures.

REVIEW

# Measurement and reversal of the direct oral anticoagulants

Bethany T. Samuelson [a], Adam Cuker [b,*]

[a] Division of Hematology, Department of Medicine, University of Washington, 1100 Fairview Ave N D5-100, Seattle, WA 98109, USA
[b] Department of Medicine and Department of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, 3400 Spruce Street, PA 19104, USA

## Practice points

- Calibrated dilute thrombin time and ecarin-based assays are the tests of choice for the measurement of dabigatran.
- Calibrated anti-Xa activity assays are the tests of choice for the measurement of rivaroxaban, apixaban, and edoxaban.
- Most DOAC-related bleeding can be managed with supportive care alone.
- Idarucizumab is the agent of choice if the reversal of dabigatran is required.
- We suggest PCC 50 IU/kg for the reversal of factor Xa inhibitors, although high-quality evidence is lacking.
- Specific reversal agents for factor Xa inhibitors are in clinical development.

## Research agenda

- Develop assays that accurately measure DOACs and can be made widely available.
- Define the efficacy and safety of specific reversal agents for the DOACs

Contents lists available at ScienceDirect

Blood Reviews

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

# Accepted Manuscript


Laboratory Assessment of the Anticoagulant Activity of Direct Oral Anticoagulants (DOACs): A Systematic Review

Bethany T. Samuelson, MD, Adam Cuker, MD, Deborah M. Siegal, MD, Mark Crowther, MD, David A. Garcia, MD

**Laboratory Assessment of the Anticoagulant Activity of Direct Oral Anticoagulants (DOACs): A Systematic Review**
**Short Title: Laboratory Assessment of DOACs**

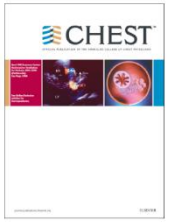
- 112 lavori sulla relazione tra livelli di farmaco e risultati di esami di laboratorio

- 35 dabigatran
- 50 rivaroxaban
- 9 apixaban
- 13 edoxaban

Accepted Manuscript

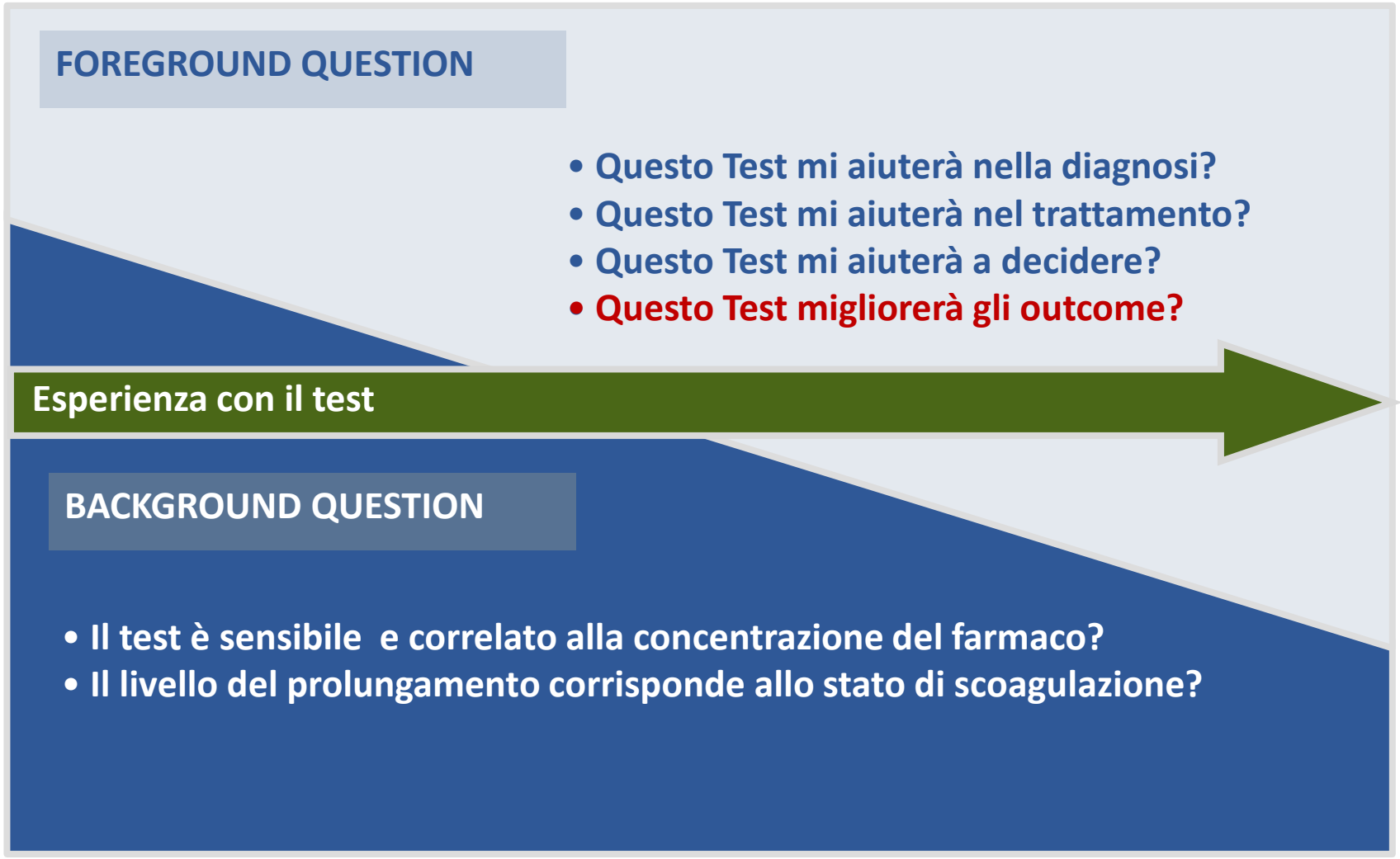
Laboratory Assessment of the Anticoagulant Activity of Direct Oral Anticoagulants (DOACs): A Systematic Review

Bethany T. Samuelson, MD, Adam Cuker, MD, Deborah M. Siegal, MD, Mark Crowther, MD, David A. Garcia, MD




- **Conclusions** Unfortunately, an ideal test, offering both accuracy and precision for measurement of any DOAC is not widely available.
- We recommend the use of a dilute **thrombin time assay** or **ecarin-based assay** for assessment of the anticoagulant effect of **dabigatran** and **anti-Xa assays** with drug-specific calibrators for assessment of the anticoagulant effects of **direct Xa inhibitors**.
- In the absence of these tests:
  - **thrombin time** or **APTT** are recommended over PT/INR for assessment of **dabigatran** and
  - **PT/INR** is recommended over APTT for detection of **factor Xa inhibitors**.
- Time since last dose, the presence or absence of drug interactions, renal and hepatic function should impact clinical estimates of anticoagulant effect in a patient for whom laboratory test results are not available.

# Background & Foreground question



# Decreto appropriatezza


Condizioni di erogabilità o indicazioni di appropriatezza prescrittiva alle prestazioni di assistenza specialistica ambulatoriale (*legge n. 125 del 6 agosto 2015*)

| numero nota | note dm 1996 | codice prestazione | PRESTAZIONI DI SPECIALISTICA AMBULATORIALE | CONDIZIONI DI EROGABILITA' | INDICAZIONI DI APPROPRIATEZZA PRESCRITTIVA |
|---|---|---|---|---|---|
| 87 | | 90.63.1 | EPARINA (Mediante dosaggio inibitore fattore X attivato) | **In emergenza emorragica con sospetto sovradosaggio di eparina a basso peso molecolare o di Xabani** | |

| numero nota | note dm 1996 | codice prestazione | PRESTAZIONI DI SPECIALISTICA AMBULATORIALE | CONDIZIONI DI EROGABILITA' | INDICAZIONI DI APPROPRIATEZZA PRESCRITTIVA |
|---|---|---|---|---|---|
| 78 | R | 90.46.4 | ALFA 2 ANTIPLASMINA | Indagine di II livello per la diagnosi di diatesi emorragiche | |
| 85 | | 90.58.3 | BETA TROMBOGLOBULINA | | esame obsoleto |
| 87 | | 90.63.1 | EPARINA (Mediante dosaggio inibitore fattore X attivato) | In emergenza emorragica con sospetto sovradosaggio di eparina a basso peso molecolare o di Xabani | |
| 94 | | 90.69.5 | INIBITORE ATTIVATORE DEL PLASMINOGENO (PAI I) | | esame obsoleto |
| 95 | | 90.75.4 | TEMPO DI PROTROMBINA (PT) | | A) Indagine di I livello per la prevenzione e la profilassi della trombosi venosa.;<br>B) Ausilio diagnostico nell'identificazione delle malattie emorragiche;<br>C) Utile nel monitoraggio dei farmaci anticoagulanti orali. |
| 96 | | 90.76.1 | TEMPO DI TROMBOPLASTINA PARZIALE (PTT) | | Indagine di I livello che contribuisce ad identificare episodi emorragici e più raramente trombotici. Utile anche come screening per la presenza di anticorpi antifosfolipidi e nel monitoraggio della terapia anticoagulante con Eparina standard non a basso PM. |
| 98 | | 90.77.2 | TEST DI RESISTENZA ALLA PROTEINA C ATTIVATA | Per inquadramento diagnostico-terapeutico delle diatesi trombofiliche congenite | |
| 136 | R | 91.29.2 | ANALISI DEL DNA PER POLIMORFISMO Con reazione polimerasica a catena, digestione enzimatica ed elettroforesi | Per le patologie e condizioni riportate nell'Allegato GENETICA (colonna A, colonna C e colonna E), su prescrizione specialistica. | In caso di utilizzo per analisi di farmacogenetica, se ne raccomanda l'uso solo su indicazioni EMA/AIFA |

# Conclusioni

- Lavorare con i clinici, come i clinici
  **(MEDICINA DI LABORATORIO)**
- Lavorare per i pazienti
  **(OUTCOMES)**
- Valutare con senso critico e cercare le prove
  **(EBM)**
- Associare clinica e ricerca, per la revisione continua dei processi diagnostici e di monitoraggio
  **(APPLY – ASSESS)**

**Davide Giavarina**

davide.giavarina@ulssvicenza.it