Warfarin Dosing

Presented by:
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Senior Principal Clinical Pharmacist
Department of Pharmacy
Singapore General Hospital
Case 1: 76 year old patient with PMH of: DM, HTN, CKD, Gout, PUD, TKR
Newly diagnosed R LL DVT in Feb ‘12 – started warfarin on 06/02/12
HAS-BLED score= 4 (high risk of bleeding)

<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
<th>Warfarin Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>06/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>07/02/2012</td>
<td>1.03</td>
<td>5</td>
</tr>
<tr>
<td>08/02/2012</td>
<td>1.12</td>
<td>7</td>
</tr>
<tr>
<td>09/02/2012</td>
<td>1.71</td>
<td>7</td>
</tr>
<tr>
<td>10/02/2012</td>
<td>2.98</td>
<td>5 (discharge)</td>
</tr>
<tr>
<td>11/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>12/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>13/02/2012</td>
<td>5</td>
<td></td>
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<tr>
<td>14/02/2012</td>
<td>5</td>
<td></td>
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<td>15/02/2012</td>
<td>5</td>
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<td>16/02/2012</td>
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<td>17/02/2012</td>
<td>5</td>
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<tr>
<td>18/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>19/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>20/02/2012</td>
<td>9.27</td>
<td>f/u at Outpatient</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
<th>Warfarin Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/03/2012, 10pm</td>
<td>&gt; 10 @ A&amp;E</td>
<td></td>
</tr>
<tr>
<td>10/03/2012, 10am</td>
<td>&gt;10</td>
<td></td>
</tr>
<tr>
<td>09/03/2012, 9pm</td>
<td>&gt;10</td>
<td></td>
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</tbody>
</table>
### Other Re-hospitalisation data

#### Rates of bleeding during 1st 30 days of therapy

Population-based cohort (Ontario); 125,195 patients with AF ≥ 66 yr old between 1997 - 2008

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>First 30 days</th>
<th>Remainder of 5 yr follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate of Bleed; % per person-year</td>
<td></td>
</tr>
<tr>
<td>All Bleeds</td>
<td>11.3 %</td>
<td>11.8</td>
</tr>
<tr>
<td>Intracranial</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>Upper GI</td>
<td>4.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Lower GI</td>
<td>4.6</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Gomes et al. CMAJ 012; DOI:10.1503/cmaj.121218
Warfarin Dosing

1. Dosing at Initiation phase
2. Dosing at maintenance phase
Warfarin—Indications

Get it rights !!!

- Prophylaxis and/or treatment of:
  - Venous thrombosis and its extension
  - Pulmonary embolism

- Prevention of Thromboembolic complications associated with AF and/or cardiac valve replacement

- Reduce risk of death, recurrent MI, and thromboembolic events such as stroke or systemic embolization after MI

- Warfarin does NOT dissolve clots that have already formed.
- Warfarin stabilize the clots so that it will not grow bigger, i.e. prevent clot extension, prevent embolism.
- Letting our body natural process eg plasminogen to dissolve the clots and our macrophages to engulf the clots which will take at least 3 to 6 months.
Recommended Therapeutic Range for Oral Anticoagulant Therapy

<table>
<thead>
<tr>
<th>Indication</th>
<th>INR</th>
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<tbody>
<tr>
<td>Venous thromboembolism (including pulmonary embolism)</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>Thromboembolic complications associated with:</td>
<td></td>
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<tr>
<td>Atrial fibrillation</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>Bioprosthetic heart valves</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>Mechanical heart valves</td>
<td>2.5–3.5</td>
</tr>
<tr>
<td>Post-myocardial infarction</td>
<td>2.5–3.5</td>
</tr>
</tbody>
</table>

Note: an INR of greater than 4.0 appears to provide no additional therapeutic benefit in most patients and is associated with a higher risk of bleeding.
Warfarin Dosing

1. Dosing at Initiation phase
Warfarin -PK

- Racemic mixture of the R- and S-enantiomers.
- The S-enantiomer exhibits 2-5 X times more anticoagulant activity than the R-enantiomer

**Absorption:** Completely absorbed, peak concentration within the first 4 hours.
Onset of anticoagulation effect: 24 hours,
Peak anticoagulant effect may be delayed 72 to 96 hours (3-4 days)
Duration of action of a single dose of racemic warfarin is 2 to 5 days.

**Distribution:** Approximately 99% plasma proteins bound. Vd 0.14 L/kg.

**Metabolism:** Metabolise in liver via cytochrome P-450 to inactive metabolites.
Isozymes include 2C9, 2C19, 2C8, 2C18, 1A2, and 3A4.
Warfarin –S enantiomer mainly metabolised by Cyp 2C9 isozyme

**Excretion:** excretion is in the form of metabolites.
Very little warfarin is excreted unchanged in urine.
The terminal half-life of warfarin after a single dose is approx 1 wk.
Effective half-life ranges from 20 to 60 h, with a mean of about 40 h.
Warfarin act by inhibiting the synthesis of vitamin K dependent clotting factors, which include Factors II, VII, IX and X, and the anticoagulant proteins C and S. Therapeutic doses of warfarin decrease the total amount of the active form of each vitamin K dependent clotting factor made by the liver by approximately 30% to 50%.

Anticoagulation Symposium & Workshop 2015
Synthesis of Dysfunctional Coagulation Factors, reduction by 30% to 50%.

Warfarin has no effect on these factors that are already formed.

Full therapeutic action is delayed until circulating coagulation factors are removed by normal degradation.

The S > R 2-5 x more anticoagulant activity but generally has a more rapid clearance. S enantiomer is metabolized primarily by the CYP2C9 enzyme of the cytochrome P450 system.
<table>
<thead>
<tr>
<th>Protein</th>
<th>Half Life</th>
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<tbody>
<tr>
<td>Factor VII</td>
<td>4 - 6 hours</td>
</tr>
<tr>
<td>Factor IX</td>
<td>24 hours</td>
</tr>
<tr>
<td>Factor X</td>
<td>48–72 hours</td>
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<tr>
<td>Factor II</td>
<td>60 hours</td>
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<tr>
<td>Protein C</td>
<td>8 hours</td>
</tr>
<tr>
<td>Protein S</td>
<td>30 hours</td>
</tr>
<tr>
<td>Warfarin</td>
<td>40 hours (range 20-60 h)</td>
</tr>
</tbody>
</table>

Chart 1: Comparisons between half-lives of Clotting factors and Warfarin
Loading dose vs Maintenance dose

Hypercoagulable states and the need to overlap for 5 days.
Warfarin Dosing Key Points:

- Patients receiving warfarin for the first time should begin at the patient's estimated average daily dose (typically 5 mg/day; range 2.5-7.5 mg/day), with a recheck of the INR in two to three doses.

- Steady-state INR values will not be realized for up to three weeks following a dose adjustment.

- Testing should be obtained before initiation of warfarin:
  - Complete blood count (CBC)
  - Platelet count
  - INR
  - aPTT
  - Creatinine
  - Liver enzymes (ALT, AST, GGT)
  - Albumin
**Warfarin Therapy Guide**

**Patient’s Sticky Label**

- **Indications for Use:**
  - AF / Mechanical Valve / Bioprosthetic Valve / Intracardiac thrombus / DVT / PE / Others:
- **Intended duration:** Lifelong / _______ Months
- **Target INR:** 2.0-3.0 / 2.5-3.5 / others:

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**Initiation of Warfarin**

**Target INR:** 2.0-3.0

<table>
<thead>
<tr>
<th>Day</th>
<th>INR</th>
<th>Warfarin Dose (mg) For &lt; 70 Years</th>
<th>Warfarin Dose (mg) For &gt; 70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;1.4</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>&lt;1.8</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>&gt;1.8</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>3</td>
<td>&gt;1.2</td>
<td>6 to 8</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>&gt;1.5</td>
<td>3</td>
<td>3</td>
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<tr>
<td></td>
<td>&gt;1.75</td>
<td>2</td>
<td>2</td>
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<td></td>
<td>&gt;2.0</td>
<td>2</td>
<td>2</td>
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<tr>
<td></td>
<td>&gt;2.5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&gt;3.0</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td></td>
<td>&gt;3.5</td>
<td>Ommit 1 day then 1mg</td>
<td>Ommit 1 day then 1mg</td>
</tr>
<tr>
<td></td>
<td>&gt;4.0</td>
<td>Ommit 2 days then 0.5mg</td>
<td>Ommit 2 days then 0.5mg</td>
</tr>
</tbody>
</table>

**Precautions during Initiation of Warfarin**

- Assess each patient for sensitivity to warfarin and adjust dose. Risk of over anticoagulation and bleeding is increased with the following:
  - Age > 70
  - Weight < 50K
  - Baseline INR > 1.4 or low platelet count (<50K)
  - History of falls or BGT
  - Severe CCF or liver disease
  - Presence of Malignancy
  - Malnutrition
  - Major surgery within 10-14 days
  - Drug interactions (e.g. Amiodarone, NSAID)
  - HAS-BLED score ≥ 3

**HAS-BLED Score**

- Hypertension >160/90mmHg
- Abnormal renal/liver disease (1 point each)
- Stroke
- Bleeding tendency/predisposition
- Labile INR’s (if on warfarin)
- Elderly (>65)
- Drug or Alcohol (1 point each)

**Management of Over-Anticoagulation**

No significant bleeding and low bleeding risk:

- INR 1-4.5: Withhold warfarin and check INR after 24 hours.
- INR 4.6-6: Omit next 1-2 doses and check INR after 24 hours. Alternatively, give vitamin K 1-3mg PO.
- INR >6: Omit warfarin and give Vitamin K 3-5mg PO. Recheck INR after 6 hours then daily for 3 days. Half-life of Vitamin K is less than that of warfarin; further doses may be needed if INR remains high.

Severe bleeding:

- Omit warfarin and give Vitamin K 5-10mg IV.
- Call hematologist on-call for approval and dosage recommendation, then give 4-factor prothrombin complexes.

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**Recommended Schedule**

- Acute PE or DVT: overlap warfarin with LMWH for a minimum of 5 days. Stop LMWH after INR has reached therapeutic levels for 2 consecutive days.
- Chronic AF: Start warfarin alone. An overlap with LMWH may be used if clinically indicated.
- Post-operative: Re-start with their usual pre-operative maintenance dose—do not re-load.

**Patient Checklist**

- Warfarin Counselling
  - INR record book
  - Warfarin VCD (English, Mandarin, Malay)
  - Follow-up for appointment after discharge:
    - Date/Time:
    - Clinic:
    - Physician:

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*For any referrals or enquiries regarding anticoagulation matters please contact SGH Pharmacist-directed Inpatient Anticoagulation Service (IPACS) at Tel: 5622 8229, Ext. 51 5506/9480 (Monday to Friday 9-6pm)*

Last Updated: 22 Aug 2014
If risk of bleeding is higher than thrombosis, start at lower dose eg 2mg, 2mg, and closely monitor the INR and any possible sign and symptoms of bleeding.

### INITIATION OF WARFARIN

**Target INR: 2.0-3.0**

<table>
<thead>
<tr>
<th>Day</th>
<th>INR</th>
<th>Warfarin Dose (mg)</th>
<th>For &lt; 70 Years</th>
<th>For &gt; 70 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;1.4</td>
<td>5</td>
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<td></td>
</tr>
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<td></td>
<td>1.8</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;1.8</td>
<td>Nil</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>&lt;1.2</td>
<td>6 to 8</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.2-1.5</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.5-2.0</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.0-3.0</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;3.0</td>
<td>Nil</td>
<td>Nil</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>&lt;1.3</td>
<td>6</td>
<td>4</td>
<td></td>
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<tr>
<td></td>
<td>1.3-1.5</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.5-1.7</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.7-2.0</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;4.0</td>
<td>Nil</td>
<td>Nil</td>
<td></td>
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</tbody>
</table>

### PRECAUTIONS DURING INITIATION OF WARFARIN

- Assess each patient for sensitivity to warfarin and adjust dose. Risk of over anticoagulation and bleeding is increased with the following:
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  - Weight < 50kg
  - Baseline INR > 1.4 or low platelet count (<50K)
  - History of falls or BGIT
  - Severe CCF or liver disease
  - Presence of Malignancy
  - Malnutrition
  - Major surgery within 10-14 days
  - Drug interactions (e.g. Amiodarone, Rifampicin)
  - HAS-BLED score ≥ 3

### HAS-BLED SCORE

- Hypertension >160mmHg: 1
- Abnormal renal/liver disease (1 point each): 1 or 2
- Stroke: 1
- Bleeding tendency/predisposition: 1
- Labile INRs (if on warfarin): 1
- Elderly (>65): 1
- Drug or Alcohol (1 point each): 1 or 2
### Anticoagulation Symposium & Workshop 2015

**IBD NEPROTIC SYNDROME SEPSIS**

**PROTEIN S FACTOR V LEIDEN (70-140%) CHADS 2 SCORE (HIGHLIGHT ACCORDINGLY) CHA 2DS-VASC 2**

**TREATMENT PARAMETERS**

<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
<th>WARF-ARIN Dose</th>
<th>LMWH/HEP Dose</th>
<th>VIT K Dose</th>
<th>Scr/CrCl</th>
<th>ALB (32-103)/ (3-36)/ (5-15)</th>
<th>ALP/ALT/AST (20-100)/ (7-36)/ (15-33)</th>
<th>HB (12-16)</th>
<th>TW (4-10)</th>
<th>PLT (140-440)</th>
<th>APTT (27-36.1)</th>
<th>PT</th>
<th>RXA</th>
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**HOSPITAL DAILY PROGRESS NOTE**

**ADMISSION DATE**

**REFERRAL DATE**

**DISCHARGE DATE**

**PRESENTING ILLNESS**

**PAST MEDICAL HISTORY**

**HYPERCOAGULABLE STATE (VIRCHOW'S TRIAD)**

<table>
<thead>
<tr>
<th>MALIGNANCY</th>
<th>PREGNANCY</th>
<th>OESTROGEN THERAPY</th>
<th>IBD</th>
<th>NEPROTIC SYNDROME</th>
<th>SEPSIS</th>
<th>TRAUMA</th>
<th>SURGERY OF LOWER EXTREMITY</th>
<th>THROMBOPHILA (REFER BELOW)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

**THROMBOPHILA SCREEN**

<table>
<thead>
<tr>
<th>TYPES:</th>
<th>HOMO-CYSTINE</th>
<th>PROTEIN C</th>
<th>PROTEIN S</th>
<th>ANTI THROMBIN III</th>
<th>FACTOR V LEIDEN</th>
<th>ANTI ACA IgM</th>
<th>ANTI ACA IgG</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORMAL RANGE:</td>
<td>(&lt;1 UI/L)</td>
<td>(65-140%)</td>
<td>(70-140%)</td>
<td>(80-120)</td>
<td>12.5-20 mpl indeterminate, 20-80 low to medium +, &gt;80 high+</td>
<td>15-20 mpl indeterminate, 20-80 low to medium +, &gt;80 high+</td>
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**VASCULAR INJURY**

<table>
<thead>
<tr>
<th>TRAUMA / SURGERY</th>
<th>HEART VALVE DX</th>
<th>ATEROESCLEROSIS</th>
<th>INDWELLING CATHETERS</th>
<th>VENEPUNCTURE</th>
<th>CHEMICAL IRRITATION</th>
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</table>

**CIRCULATORY STASIS**

<table>
<thead>
<tr>
<th>LEFT VENTRICULAR DYSFUNCTION</th>
<th>IMMOBILITY</th>
<th>VENOUS INSUFFICIENCY</th>
<th>VENOUS OBSTRUCTION</th>
<th>ATRIAL FIBRILLATION (CALC CHADS2 SCORE BELOW)</th>
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**CHADS 2 SCORE (HIGHLIGHT ACCORDINGLY)**

<table>
<thead>
<tr>
<th>RISK:</th>
<th>CHF</th>
<th>HTN</th>
<th>AGE &gt;75</th>
<th>DM</th>
<th>STROKE +2</th>
<th>SCORE:</th>
<th>VASCULAR DX +1</th>
<th>FEMALE +1</th>
<th>AGE 65 - 74 +1 ; AGE &gt;75 +2</th>
<th>TOTAL CHADSVASC SCORE:</th>
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**HASBLED SCORE**

<table>
<thead>
<tr>
<th>HTN</th>
<th>ABNORMAL RENAL / LIVER FN</th>
<th>STROKE</th>
<th>BLEEDING</th>
<th>LABILE INR</th>
<th>ELDERLY &gt; 65</th>
<th>DRUG OR ALCOHOL</th>
<th>OTHERS:</th>
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**BLEEDING RISK ASSESSMENT**

<table>
<thead>
<tr>
<th>HTN</th>
<th>ABNORMAL RENAL / LIVER FN</th>
<th>STROKE</th>
<th>BLEEDING</th>
<th>LABILE INR</th>
<th>ELDERLY &gt; 65</th>
<th>DRUG OR ALCOHOL</th>
<th>OTHERS:</th>
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**ANTICOAGULATION PLANS**

**TARGET INR:**

**DATE/ DUPLEX SCAN/SPIRAL CT/D-DIMER:**

**DURATION:**

**MONITORING PARAMETERS**

<table>
<thead>
<tr>
<th>DATE</th>
<th>INR</th>
<th>WARF-ARIN Dose</th>
<th>LMWH/HEP Dose</th>
<th>VIT K Dose</th>
<th>Scr/CrCl</th>
<th>ALB (32-103)/ (3-36)/ (5-15)</th>
<th>ALP/ALT/AST (20-100)/ (7-36)/ (15-33)</th>
<th>HB (12-16)</th>
<th>TW (4-10)</th>
<th>PLT (140-440)</th>
<th>APTT (27-36.1)</th>
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**REMARKS (BLEEDING, THROMBOSIS, DIET, INTERACTING DRUGS)/RECOMMENDATION**

**INVTVN ACCEPTED? (Y/N):**
### GUIDE ON INTERACTING DRUGS

<table>
<thead>
<tr>
<th>DRUG</th>
<th>REACTION</th>
<th>RECOMMENDATIONS</th>
<th>DRUG</th>
<th>REACTION</th>
<th>RECOMMENDATIONS</th>
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<tbody>
<tr>
<td>Co-trimoxazole</td>
<td>Generally see INRs in the 8-20 range</td>
<td>Decrease dose by 20-30%</td>
<td>Carbamazepine</td>
<td>Dependent on dose and time frame, often INR</td>
<td>Increase dose by 30%</td>
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<td>1.0 - 1.5</td>
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<tr>
<td>Fluconazole (&gt;1dose)</td>
<td>Have seen INRs 15 - 30</td>
<td>Decrease dose 30 - 40%</td>
<td>Rifampicin</td>
<td>INR = 1.0</td>
<td>Double or Triple dose</td>
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<td>Amiodarone</td>
<td>Dose and time dependent, INR in 8-20 range</td>
<td>At 2 weeks intervals, decrease the dose by approximately 5-10%, usually a total 30-50% is needed</td>
<td>Phenobarbitone</td>
<td>Dependent on number of doses taken - generally</td>
<td>Continuous use: Increase dose by 20%; adjust INR to upper end of range for intermittent use</td>
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<tr>
<td>Aspirin</td>
<td>INR usually 6-10</td>
<td>Avoid/stop Aspirin and adjust dose as for any high INR</td>
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<tr>
<td>Metronidazole</td>
<td>Variable - not much change in patient with chronic diarrhoea or UC; others INR may increase 18-20</td>
<td>Decrease dose by 10% and reassess within 3-4 days</td>
<td>Primidone</td>
<td>Dependent on dose, INR subtherapeutic to 1.0</td>
<td>Increase the dose by 10% to 40% dependent on INR response</td>
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### WARFARIN/LMWH COUNSELLING

**START DATE** | **STOP DATE** | **MEDICINE/ DOSE** | **START DATE** | **STOP DATE** | **MEDICINE/ DOSE** |
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### SINGAPORE GENERAL HOSPITAL: INPATIENT ANTICOAGULATION SERVICE (IPACS)

**START DATE** | **STOP DATE** | **MEDICINE/ DOSE** | **START DATE** | **STOP DATE** | **MEDICINE/ DOSE** |
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**INCREASE INR**

**DECREASE INR**
RECOMMENDED SCHEDULE

Acute PE or DVT: overlap warfarin with LMWH
Chronic AF: Start warfarin alone. An overlap with LMWH may be used if clinically indicated.
Post-operative: Restart with their usual pre-operative maintenance dose- Do not re-load

PATIENT CHECKLIST

☐ Warfarin Counselling
☐ INR record book
☐ Warfarin VCD (English, Mandarin, Malay)
☐ Follow-up for appointment after discharge
  • Date/ Time:____________________
  • Clinic: ______________________
  • Physician:____________________
In general

- INR therapeutic after 3 days of warfarin -> halve dose
- Eg. 5mg, 5mg, 5mg -> INR 2.41 -> 2.5mg
- Eg. 3mg, 3mg, 3mg -> INR 2.41 -> 1.5mg

- Use average weekly dose
- Eg. 5mg, 5mg, 8mg, 8mg, 6mg, 6mg, 7mg -> 2.32 -> 45mg/7=6.45mg -> 6mg
- Remember! Up to 3 weeks on same dose before full response
In general, (initiation)

- INR trends – upwards / downwards
  - Close monitoring is required, eg 2-3x/wk
  - Acceptable INR increase < 0.3 / day
  - May take 2-3 days for dose changes to affect INR
    - Onset 24 hour, peak effect: 72-96 hours (3-4 days)
  - Steady state: 2-3 weeks later
    - \( 5 \times T_{1/2} = 5 \times 60\text{hr} \text{ (prothrombin)} = 300 \text{ hour} = 12.5 \text{ days} \)

- Off heparin or LMWH when INR is therapeutic after 5 days of treatment for VTE.

- Check daily or alternate day (during inpatient stay)
Continual Monitoring plan

- **Warfarin**: INRs, Hb, F/U plan, ideal TCU 2-3 days post discharge
- **LMWH**: CrCL, Hb, Platelet (weekly, if possible)

- **INR >4** --> daily INR

- **Interacting medicines:**
  - **Increase INR**: Metronidazole, Co-trimoxazole, Fluconazole, Ciprofloxacin, Erythromycin, Clarithromycin, NSAIDs, Ceftriazone, Amiodarone, Allopurinol, Statins & Fibrates
  - **Decrease INR**: Rifampicin, Carbamazepine, Phenytoin, Primidone
  - **Increase / Decrease INR**: Thyroid replacement and anti-thyroid therapy

- **Acute illness**
  - infection, diarrhoea, vomiting, fever,
  - loss of appetite, Nil By Mouth (NBM), malnutrition, low albumin
  - Change in milk feeds (Vitamin K content)
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<th>Drugs</th>
<th>Reaction</th>
<th>ACNA Warfarin Adjustment</th>
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<tr>
<td><strong>Increase</strong></td>
<td>Co-trimoxazole (Bactrim, Septrin)</td>
<td>Generally see INRs in the 8-20 range</td>
<td>Decrease dose 20-30%</td>
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<td>Fluconazole (more than one dose)</td>
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<td>Variable - not much change in patient with chronic diarrhea or UC; others INR may increase to 8-20 range</td>
<td>Decrease dose by 10% and reassess within 3-4 days</td>
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<td><strong>Decrease</strong></td>
<td>Phenobarbitone</td>
<td>Dependent on number of doses taken - generally INR 1.0 -1.4</td>
<td>Increase dose by 20% for continuous use; adjust INR to upper end of range for intermittent use</td>
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<tr>
<td></td>
<td>Rifampicin</td>
<td>INR = 1.0</td>
<td>Double or Triple dose</td>
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<td></td>
<td>Carbamazepine</td>
<td>Dependent on dose and time frame, often INR 1.0 -1.5</td>
<td>Increase dose by 30%</td>
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<tr>
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<td>Primidone (Mysoline)</td>
<td>Dependent on dose, INR subtherapeutic to 1.0</td>
<td>Increase the dose by 10% to 40% dependent on INR response</td>
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</table>
Continual Monitoring plan

- Warfarin: INRs, Hb trend, F/U plan
- LMWH: CrCL, Hb, Platelet trend

Over-Anticoagulation

- Assess Bleeding vs Thrombotic risk
- Identify cause or contributory factor
- Omit warfarin
  - Oral Vitamin K (dilute from injection)
    - Onset 6-10 hrs, Peak 24-48 hrs
  - IV Vitamin K
    - Onset 1-2 hrs, Peak 12-14 hrs
- IV FFP 15ml/kg (bleeding or quick reversal),
  - FFP works faster than Vit K, but shorter duration of action
  - Ie INR may rebound if Vitamin K not given
- Recheck INR in 6 hours if needed

MANAGEMENT OF OVER-ANTICOAGULATION

<table>
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<th>INR</th>
<th>Action</th>
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<tr>
<td>4-5</td>
<td>Withhold warfarin and check INR after 24 hours.</td>
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<tr>
<td>5-9</td>
<td>Omit next 1-2 doses and check INR after 24 hours. Alternatively, give Vitamin K 1-3mg PO</td>
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<tr>
<td>&gt;9</td>
<td>Omit warfarin and give Vitamin K 3-5mg PO. Recheck INR after 6 hours then daily for 3 days. Half-life of Vitamin K is less than that of warfarin; further doses may be needed if INR remains high</td>
</tr>
</tbody>
</table>

Severe bleeding

| INR >1.5 | Omit warfarin and give Vitamin K 5-10mg IV. Call hematologist on-call for approval and dosage recommendation, then give 4 factor prothrombin complexes |
Warfarin Dosing (Maintenance Phase)
Dosing Considerations

- **Initial**
  - 2–5mg per day
  - Dosage adjustments based on PT/INR determinations
  - Large loading dose may increase the incidence of hemorrhagic complications

- **Maintenance**
  - 0.5 –10 mg daily
  - Individual dose and interval should be gauged by the patient’s PT/INR response

- **Duration of therapy**
  - Individualized
General Principles of Warfarin Dosing

- Significant increase in thromboembolism as INR values decrease below 1.7.
- The bleeding risk increases substantially at INR above 5.
- Clinical risk and past medical history should be considered in all dosing decisions.
- Prescription and over-the-counter medications can adversely affect the INR response to warfarin.
- Herbal or natural remedies can change the INR response to warfarin and/or increase a patient’s risk of bleeding.
- In these instances, additional monitoring may be needed.
- Food that contains moderate amounts of Vitamin K can decrease the INR response to warfarin.
- Patients should maintain a consistent diet.
- PTR above 2.0 (INR of 3.7 to 4.3) increases the risk of bleeding.
- The estimated odds ratio of subdural hemorrhage increased 7.6 fold as the PTR increased from 2.0 to 2.5.

• Stopping 1 day of warfarin, INR could reduce in average of 0.26 (range from 0.2 - 0.5), from our local INR normalization study
• Stopping 1 day of warfarin, INR could reduce in average of 0.26 (range from 0.2 - 0.5), from our local INR normalization study
Dosing Considerations

- Institute for Clinical Systems Improvement Health Care guideline,
  - Expect a 15% dose adjustment to result in an approximately 1.0 INR change.
  - Likewise, a 10% dose adjustment will result in an approximate 0.7-0.8 INR change.

- For our local population, there is a trend towards
  - 10% weekly dose / 1 INR, or
  - 1% weekly dose / 0.1 INR
  - This is just a rough guide !!!

- Stopping 1 day of warfarin, INR could reduce in average of 0.26 (range from 0.2 - 0.5), from our local INR normalization study
TITLE: Review of Warfarin Dose Titration Patterns at National Heart Centre of Singapore.

Introduction and Objective
Warfarin therapy is the gold standard in stroke reduction for atrial fibrillation (AF) patients. Achieving its therapeutic goal remains highly unpredictable and dependent on prescribers’ experience. This study aims to review warfarin dose titration patterns at the National Heart Centre of Singapore (NHCS) and correlate weekly dose changes to the International Normalized Ratio (INR) changes.

Methods
This is a retrospective study from January 2012 to December 2014. Data was collected from Sunrise Clinical Manager. Patients had warfarin therapy for non-valvular AF with INR out-of-range unaccounted for and a dosage change followed by stabilised INR for at least two clinic visits. Percentage change in weekly dose was correlated with INR change using a simple linear regression model, with R-value computed.

Results
Sixty-seven patients (47.8% male) were recruited, with a mean age of 70 ± 10 years. 91.0% were Chinese; 83.6% had a target INR range 2.0 to 3.0. INR before dose titration ranged from 1.5 to 4.0. Fifty-two percent of patients were followed up with within one month. An equation of % weekly dose change = 9.1426(INR change) + 0.1501 was derived (R=0.802). Correlation between INR change and weekly dose change is weak when the dose change is above 15% (R=0.328).

Conclusion
Titration of warfarin dose is related to the INR change. An estimated change in 10% of weekly dose corresponds to an approximately 1.08 change in INR. This calculated value may not be applicable for the weekly dose change above 15%. Further investigation is required to explain possible factors affecting INR change at higher percentage of weekly dose change.

(262 words)
67 patients, 47.8% male, mean age: 70 ± 10 years, Chinese: 91%

Target INR: 2-3 (83.6%)

INR before dose titration: 1.5-4.0

52% patients were followed up within 1 month.

% weekly dose change = 9.1426 (INR change) + 0.1501  \quad (R=0.802)

Rearranging the equation:

INR change = (% weekly dose change – 0.1501 )/ 9.1426

Correlation is weekly when dose change is > 15%  \quad (R=0.328)

Raw data analysis from Ms Hon JS and team from NHCS
% weekly dose change = 9.1426 (INR change) + 0.1501 \ (R = 0.802)

INR change = (% weekly dose change − 0.1501) / 9.1426

n = 67 patients, 
Age : 70 ± 10 years, 
Chinese : 91% 
Target INR : 2-3 (83.6%) 
INR before dose titration : 1.5-4.0

Correlation is weekly when dose change is > 15\% \ (R=0.328)
ACC Checklist - Questionnaires

- Bleeding?
- Thrombosis?
- Change in Diet?
- Medication Change? Eg paracetamol, NSAIDs, Abx
- Herbal product eg Ginseng, Cordycep
- Illness? eg hyperthyroid, fever, diarrhea
- Hospital / Emergency?
- Physical activity / Exercise / Lifestyle eg stress
- Smoking / Alcohol
- Compliance
- INR results – within range $\pm 0.3$, above or below range $>\pm 0.3$
Example 1: Subtherapeutic INR

- For eg, 40 yo Chinese pt with target INR of 2-3,
- INR today is 1.5, and previous visit is INR=1.7, and he is on 3mg om. Suppose all the parameter are stable.

- How much to adjust up for this patient today?
- Take the middle of the target range, ie 2.5
- How much INR diff = 2.5 (aim) – 1.5 (current) = 1.0,
- ie to adjust the weekly dose up by 10%
- Current weekly dose = 21mg/wk (ie 3mg om)
- Increase 10% = 23.1mg/wk, rounded to 23mg
- 23mg/week = 3mg (Mon-Fri), 4mg (Sat & Sun) x 2/52
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<th>Mon (mg)</th>
<th>Tue (mg)</th>
<th>Wed (mg)</th>
<th>Thu (mg)</th>
<th>Fri (mg)</th>
<th>Sat (mg)</th>
<th>Sun (mg)</th>
<th>Weekly Total</th>
<th>+ 1%</th>
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</table>
Example 2 : Subtherapeutic INR

Patient with warfarin 1mg od, target INR 2.5 (range 2-3)
INR today INR is 1.6. Compliant and other parameters stable.
Magnitude of adjustment : 2.5 – 1.6 = 0.9. ie to increase weekly dose by 9%.

![Warfarin Dosing Chart](chart.png)
Example 2: **Common Dosing “Error” at maintenance phase**

Increase warfarin 1mg daily to 1.5mg daily, ie from 7mg/week to 10.5mg/week

A total of 50% increase in weekly dose, and the INR can potentially increase to \((1.6 + 5) = 6.6\) → **Over Anticoagulation !!!!**
Example 2: **Common Dosing “Error” at maintenance phase**

- Do not confuse the dosing strategy used during *initiation* vs *maintenance* phase.

- Initiation dose can be increased quite dramatically, but this should not apply when patient has reached steady state.

- Adjust of warfarin maintenance dose by % weekly dose is “safer” than just adjust 0.5mg each time. Generally, in the range of 3 to 10% is sufficient.

<table>
<thead>
<tr>
<th>Mon (mg)</th>
<th>Tue (mg)</th>
<th>Wed (mg)</th>
<th>Thur (mg)</th>
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<th>Sat (mg)</th>
<th>Sun (mg)</th>
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<th>Increase of 0.5mg/day or 3.5mg/wk new weekly dose would be</th>
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<td><strong>56.0</strong></td>
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<td>6%</td>
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</table>
Example 3 – Maintenance ---- INR within range

- Target INR 2 to 3, warfarin dose 3mg/day
- No bleeding / thrombosis, no change in medicine / diet,
- No recent illness, compliance with medicines
- No change in smoking / alcohol / activity

- INR today 2.5

- What would you dose ?
Example: 3 – Maintenance ---- INR within range

- Target INR 2 to 3, warfarin dose 3mg/day

- No bleeding / thrombosis, no change in medicine / diet,
- No recent illness, compliance with medicines
- No change in smoking / alcohol / activity

- INR 2.5 is within range (target 2-3), Keep the same dose
- If 1st time in range TCU x 3 - 4/52
- If 2nd time in range, TCU x 6 - 8/52
- If 3rd time in range TCU x 8-12/52

- Always advice patient to come back early or go to A&E if any bleeding or thrombosis
• Target INR 2 to 3, warfarin dose 3mg/day

• **INR today 3.2,**

• No bleeding / thrombosis,

• No change in medicine / diet,

• No recent illness,

• Compliance with medicines

• No change in smoking / alcohol / activity

• What would you do?
Example: 4 – Maintenance – INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day,
- INR today 3.2
- No bleeding / thrombosis, no change in medicine / diet,
- No recent illness, compliance with medicines
- No change in smoking / alcohol / activity

- INR slightly above range, eg INR 3.2, which is the first time,
- INR less than 0.3 above target range
Example: 4 – Maintenance – INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day,
- INR today 3.2
  - No bleeding / thrombosis, no change in medicine / diet,
  - No recent illness, compliance with medicines
  - No change in smoking / alcohol / activity

- INR slightly above range, eg INR 3.2, which is the first time,
- INR less than 0.3 above target range

- A) Keep the same dose and observe on next TCU, or
Example: 4 – Maintenance – INR above Target Range

- **Target INR 2 to 3, warfarin dose 3mg/day,**
- **INR today 3.2**
  - No bleeding / thrombosis, no change in medicine / diet,
  - No recent illness, compliance with medicines
  - No change in smoking / alcohol / activity

- **INR slightly above range, eg INR 3.2, which is the first time,**
- **INR less than 0.3 above target range**

  - **A) Keep the same dose and observe on next TCU, or**
  - **B) Reduce the dose for 2-3 days, then maintain the same dose**
    - eg 2.5mg x 3days, then 3mg om x 2-3 /52 (weekly dose reduce by 3.6%)
Target INR 2 to 3, warfarin dose 3mg/day,

INR today 3.2

No bleeding / thrombosis, no change in medicine / diet,
No recent illness, compliance with medicines
No change in smoking / alcohol / activity

INR slightly above range, eg INR 3.2, which is the first time.

INR less than 0.3 above target range

A) Keep the same dose and observe on next TCU, or

B) Reduce the dose for 2-3 days, then maintain the same dose
   eg 2.5mg x 3days, then 3mg om x 2-3 /52 (weekly dose reduce by 3.6%)

C) Stop for 1 dose, then resume as 3mg om, tcu x 2-3 wk
Example 5: Maintenance - INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day

- **INR today: 3.5**
  - No bleeding / thrombosis,
  - No change in medicine / diet,
  - No recent illness,
  - Compliance with medicines
  - No change in smoking / alcohol / activity

- **What would you do?**
Example 5: Maintenance - INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day
- INR today: 3.5
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity

Additional information:
- Previous INR was 3.2 three weeks ago,
- Todays INR is 3.5
- IE INR above target range (2-3) for two consecutive visit

What would you do?
Example 5: Maintenance - INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day
- **INR today : 3.5**
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR above target range, eg INR 3.5 for 2 consecutive visit
- (previous INR was 3.2 three weeks ago)

- **Stop warfarin for 2 days**

- why ?
Target INR 2 to 3, warfarin dose 3mg/day

INR today : 3.5

No bleeding / thrombosis,
No change in medicine / diet,
No recent illness,
Compliance with medicines
No change in smoking / alcohol / activity
INR above target range, eg INR 3.5 for 2 consecutive visit (previous INR was 3.2 three weeks ago)

Stop warfarin for 2 days because INR decline by about 0.3/day (range 0.26 to 0.5 per day)

Stop for 2 days ie to reduce INR from 3.5 -> 3.2 -> 2.9
restart warfarin once INR is within target range (2-3) or

Stop for 3 days ie to reduce INR from 3.5 -> 3.2 -> 2.9 -> 2.6
restart warfarin once INR is within target range (2-3)

What is your new warfarin dose?
Example 5: Maintenance - INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day
- **INR today: 3.5**
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR above target range, eg INR 3.5 for 2 consecutive visit
- (previous INR was 3.2 three weeks ago)

A. Stop warfarin for 2 days, Reduce the weekly dose by 5 to 15%.
   - **Do you choose to reduce by 1%, 3%, 5%, 7%, 10%, 12%, or 15%?**
Example 5: Maintenance - INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day
- INR today: 3.5
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR above target range (2-3), eg INR 3.2 → 3.5 for 2 consecutive visit
  (previous INR was 3.2 three weeks ago)

A. Stop warfarin for 2 days

- Based on approx of reducing 1% weekly dose correspond to reduction of INR by 0.1
- 3.5 (INR today) – 2.5 (INR target) = 1.0
- ie reduce warfarin weekly dose by 10%,
- ie Reduce warfarin weekly dose from 21mg/wk to 18.9mg/wk,
- rounded up to nearest 19mg/wk, ie -9.5%,
- 2.5mg\(^4\)/3mg\(^3\) ie 2.5mg alternate with 3mg or
- 2.5 mg (Mon – Thu), 3mg (Fri – Sat) or
- 3mg (Mon – Fri), 2mg (Sat & Sun)
- Always have patient’s compliance in mind, ie check with them which one is more convenient
**Example 5: Maintenance - INR above Target Range**

Target INR 2-3, warfarin dose 3mg/day, INR today: 3.5, **reduce weekly dose by 10% to aim at inr 2.5**

---

### WARFARIN DOSING CHART

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<thead>
<tr>
<th>Mon (mg)</th>
<th>Tue (mg)</th>
<th>Wed (mg)</th>
<th>Thu (mg)</th>
<th>Fri (mg)</th>
<th>Sat (mg)</th>
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</tbody>
</table>

**INR above Target Range**

- Total dose: 20mg/week

**Date:**

- **Monday:** 17.5 mg
- **Tuesday:** 18.0 mg
- **Wednesday:** 18.5 mg
- **Thursday:** 20.0 mg
- **Friday:** 18.5 mg
- **Saturday:** 18.0 mg
- **Sunday:** 20.5 mg

**Reduced weekly dose by 10% to aim at INR 2.5:**

- **Monday:** 18.9 mg
- **Tuesday:** 18.9 mg
- **Wednesday:** 18.9 mg
- **Thursday:** 19.0 mg
- **Friday:** 19.0 mg
- **Saturday:** 18.9 mg
- **Sunday:** 18.9 mg
Example 5: Maintenance - INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day
- INR today: 3.5
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR above target range, eg INR 3.5 for 2 consecutive visit
  (previous INR was 3.2 three weeks ago)

A. Stop warfarin for 2 days
   - Based on approximation of reducing 1% weekly dose correspond to reduction of INR by 0.1
   - 3.5 (INR today) – 2.5 (INR target) = 1.0
   - ie reduce warfarin weekly dose by 10%,
   - ie from warfarin weekly dose 21mg/wk reduce to 18.9mg/wk
   - Rounded up to nearest 19mg/wk, ie -9.5%,
   - 2.5mg/ 3mg³ ie 2.5mg alternate with 3mg or
   - 2.5 mg (Mon – Thu), 3mg (Fri – Sat) or
   - 3mg (Mon – Fri ), 2mg (Sat & Sun)
   - Always have patient’s compliance in mind, and check with them which one is more convenient

When is the next TCU?
Example 5: Maintenance - INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day
- INR today: 3.5
- No bleeding / thrombosis, No change in medicine / diet, No recent illness, Compliance with medicines, No change in smoking / alcohol / activity

INR above target range, eg INR 3.2 --> 3.5 for 2 consecutive visit
(previous INR was 3.2 three weeks ago)

A. Stop warfarin for 2 days, reduce weekly dose from 21mg/wk by 10% to 19mg/wk

- Based on approximation of reducing 1% weekly dose correspond to reduction of INR by 0.1
- 3.5 (INR today) – 2.5 (INR target) = 1.0
- ie reduce warfarin weekly dose by 10%,
- ie from warfarin weekly dose 21mg/wk reduce to **18.9mg/wk**
- Rounded up to nearest 19mg/wk, ie -9.5%,
- 2.5mg/ 3mg³ ie 2.5mg alternate with 3mg or
- 2.5 mg (Mon – Thu), 3mg (Fri – Sat) or
- 3mg (Mon – Fri ), 2mg (Sat & Sun)
- Always have patient’s compliance in mind, and check with them which one is more convenient

- **TCU x 2 - 3 /52**

- (if patient bargain, up to 4/52 is ok! Not longer duration than this)

- **Always advice patient to come back early or go to A&E if any bleeding or thrombosis**
Example 5 b: Maintenance - INR above Target Range

- Target INR 2 to 3, warfarin dose 3mg/day
- INR today : 3.5
- No bleeding / thrombosis, No change in medicine / diet, No recent illness, Compliance with medicines, No change in smoking / alcohol / activity
- INR above target range, eg INR 3.2->3.5 for 2 consecutive visit, (previous INR was 3.2 three weeks ago)

**B. Stop warfarin for 2 days, reduce warfarin weekly dose by 7%**

- Based on approx of reducing 1% weekly dose correspond to reduction of INR by 0.1
- 3.5 (INR today) – 0.7 (INR reduction) = 2.8
- i.e. reduce warfarin weekly dose by 7%,
- i.e. reduce warfarin weekly dose from 21mg/wk to 19.5 mg/wk
- 2.5mg³/ 3mg⁴ i.e. 2.5mg alternate with 3mg or
- 2.5 mg (Mon – Wed), 3mg (Thu – Sat)
- Always have patient’s compliance in mind, and check with them which one is more convenient for them
- TCU x 2 - 3 /52 (notice, maximum is 3/52 tcu, do not stretch to 4/52)
- Always advice patient to come back early or go to A&E if any bleeding or thrombosis
Example 5b: Maintenance - INR above Target Range

Target INR 2-3, warfarin dose 3mg/day, INR today: 3.5, reduce weekly dose by 7% to aim at INR 2.8
Target INR 2 – 3, current warfarin dose at 3mg om or 21mg/week

- **INR today : 1.9**

- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity

- How would you dose the patient today?
Example 6a: maintenance – INR below target range

Target INR 2 – 3, current warfarin dose at 3mg om or 21mg/week

- **INR today: 1.9**
  - No bleeding / thrombosis,
  - No change in medicine / diet,
  - No recent illness,
  - Compliance with medicines
  - No change in smoking / alcohol / activity

- Additional info:
- Last INR two months ago was 2.3 → 1.9 (today)
- ie INR was in range for the last visit, but this time is slightly below target range

- How would you dose the patient today?
Target INR 2 – 3, current warfarin dose at 3mg om or 21mg/week

- **INR today : 1.9**
  - No bleeding / thrombosis,
  - No change in medicine / diet,
  - No recent illness,
  - Compliance with medicines
  - No change in smoking / alcohol / activity

- Last INR two months ago was 2.3 → 1.9 (today),
- ie INR was in range for the last visit, but this time is slightly below target range

**Choice A :** Keep the same dose, 3mg OM, TCU x 1/12

**Choice B :** Give a booster dose of 4mg x 1/7,
then maintain on same dose of 3mg OM x 1/12

TCU up to 2/12 is ok ! If patient were to bargain.
Target INR 2 – 3, current warfarin dose at 3mg OM or 21mg/week

- **INR today : 1.8**
  - No bleeding / thrombosis,
  - No change in medicine / diet,
  - No recent illness,
  - Compliance with medicines
  - No change in smoking / alcohol / activity

- **Additional info:-**
  - INR below target range for 2 consecutive visits
  - previous INR was **2.3** (3/12 ago) → **1.9** (1/12 ago) → **1.8** (today)
  - ie previous booster dose 4mg x 1/7 did not increase the INR up at all, and the INR is still decreasing

**How would you dose patient today?**
Target INR 2 – 3, current warfarin dose at 3mg OM or 21mg/week

- **INR today**: 1.8
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR below target range for 2 consecutive visits,
- INR is on decreasing trend from 2.3 ->1.9 -> 1.8 (today)

**Choice A:**  2.5 (target INR) – 1.8 (INR todate) = 0.7

- Increase weekly dose by 7%, from 21mg/wk to 22.47mg/wk
- Rounded to 22.5mg/week, ie 3.5mg³ / 3mg⁴
- 3.5mg alternate with 3mg, or
- 3.5mg (Mon to Wed), 3mg (Thu to Sun)

**When is the next TCU ?**
Target INR 2 – 3, current warfarin dose at 3mg OM or 21mg/week

- **INR today**: 1.8
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR below target range for 2 consecutive visits
- INR is on decreasing trend from 2.3 → 1.9 → 1.8 (today)

**Choice A:** 2.5 (target INR) – 1.8 (INR today) = 0.7
- Increase weekly dose by 7%, from 21mg/wk to 22.47mg/wk
- Rounded to 22.5mg/week, ie 3.5mg\(^3 \div 3\)mg\(^4\)
- 3.5mg alternate with 3mg, or
- 3.5mg (Mon to Wed), 3mg (Thu to Sun)

**When is the next TCU?**
- **TCU 2 - 3 / 52**
Example 6c: maintenance – INR below target range

Target INR 2 – 3, current warfarin dose at 3mg OM or 21mg/week

- **INR today : 1.8**
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR below target range for 2 consecutive visits
- INR is on decreasing trend from 2.3 -> 1.9 -> 1.8 (today)

**Choice B: Only increase weekly dose by 5%, from 21mg/wk to 22.05mg/wk**

ie INR expect to increase to : 1.8 (today) + 0.5 (increase of 5% wkly dose) = 2.3

Rounded to 22mg/week, ie

- 3mg (Mon to Fri), 3.5mg (Sat & Sun) or
- 3mg (Mon to Sat), 4mg (Sun) or

**Always have patient’s compliance in mind, ie check with them which regime is more convenient?**

**When is the next TCU ?**
Example 6c: maintenance – INR below target range

Target INR 2 – 3, current warfarin dose at 3mg OM or 21mg/week

- INR today : 1.8
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR below target range for 2 consecutive visits
- INR is on decreasing trend from 2.3 -> 1.9 -> 1.8 (today)

• **Choice B: Only increase weekly dose by 5%, from 21mg/wk to 22.05mg/wk**
  • ie INR expect to increase to : 1.8 (today) + 0.5 (increase of 5% wkly dose) = 2.3
  • Rounded to 22mg/week, ie
  • 3mg (Mon to Fri), 3.5mg (Sat & Sun) or
  • 3mg (Mon to Sat), 4mg (Sun) or
  • *Always have patient’s compliance in mind, ie check with them which regime is more convenient?*
  • *When is the next TCU?*

• **Since only 5% increase, TCU 2-3/52, up to 4/52 is ok!**
Example 6d: maintenance – INR below target range

Target INR 2 – 3, current warfarin dose at 3mg OM or 21mg/week

- INR today: 1.8
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR below target range for 2 consecutive visits

- INR is on decreasing trend from 2.3 -> 1.9 -> 1.8 (today)
- Choice C: increase wkly dose by 3%, from 21mg/wk to 21.63mg/wk
  ie INR expect to increase to: 1.8 (today) + 0.3 (increase of 5% wkly dose) = 2.1
- Rounded to 21.5mg/week, ie only +2.5% increase
- 3mg (Mon to Sat), 3.5mg (Sun)

- When is the next TCU?
Target INR 2 – 3, current warfarin dose at 3mg OM or 21mg/week

- **INR today : 1.8**
- No bleeding / thrombosis,
- No change in medicine / diet,
- No recent illness,
- Compliance with medicines
- No change in smoking / alcohol / activity
- INR below target range for 2 consecutive visits
- INR is on decreasing trend from 2.3 -> 1.9 -> 1.8 (today)

- **Choice C:** Only want to increase weekly dose by 3%, from 21mg/wk to 21.63mg/wk
- ie INR expect to increase to :1.8 (today) + 0.5 (increase of 5% weekly dose) = 2.3
- Rounded to 21.5mg/week, ie only +2.5% increase
- ie warfarin 3mg (Mon to Sat), 3mg (Sun)
- When is the next TCU?

**Since only 2.5% increase, TCU 2-3/52,**

**up to 4-6/52 is ok!**
Example 7: maintenance dosing

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<td>82</td>
</tr>
<tr>
<td>Indication</td>
<td>TIA secondary to AF, likely Cardioembolic stroke</td>
</tr>
<tr>
<td>Target INR</td>
<td>2 to 2.5</td>
</tr>
<tr>
<td>Duration</td>
<td>Longterm</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Visit Date</th>
<th>Target</th>
<th>Bleeding</th>
<th>Thrombosis</th>
<th>New/change in meds/diet</th>
<th>New/Recent illness</th>
<th>Non-compliance</th>
<th>Notes</th>
<th>Warfarin dose</th>
<th>TCU</th>
</tr>
</thead>
<tbody>
<tr>
<td>17/1/2007</td>
<td>2.0 to 2.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18/1/2007</td>
<td>1.43</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>19/1/2007</td>
<td>1.49</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20/1/2007</td>
<td>1.56</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3mg om</td>
<td></td>
</tr>
<tr>
<td>21/1/2007</td>
<td>2.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3mg om</td>
<td></td>
</tr>
<tr>
<td>16/2/2007</td>
<td>2.11</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>3mg om</td>
<td></td>
</tr>
<tr>
<td>15/3/2007</td>
<td>1.7</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>what could have cause this drop in INR? How much dose to increase?</td>
<td></td>
</tr>
</tbody>
</table>
### Example 7: maintenance dosing

<table>
<thead>
<tr>
<th>Name</th>
<th>TFL</th>
<th>DOB</th>
<th>01/01/1931</th>
<th>Sex</th>
<th>Female</th>
<th>Age</th>
<th>82</th>
<th>Ethnic Gp</th>
<th>Chinese</th>
<th>Indication</th>
<th>TIA secondary to AF, likely Cardioembolic stroke</th>
<th>Target INR</th>
<th>2 to 2.5</th>
<th>Duration</th>
<th>Longterm</th>
</tr>
</thead>
</table>

#### Target

<table>
<thead>
<tr>
<th>Visit Date</th>
<th>Bleeding</th>
<th>Thrombosis</th>
<th>New/change in meds/diet</th>
<th>New/Recent illness</th>
<th>Non-compliance</th>
<th>Notes</th>
<th>Warfarin dose</th>
<th>TCU</th>
</tr>
</thead>
<tbody>
<tr>
<td>17/01/2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.05</td>
<td></td>
</tr>
<tr>
<td>18/01/2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.43</td>
<td></td>
</tr>
<tr>
<td>19/01/2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.49</td>
<td></td>
</tr>
<tr>
<td>20/01/2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.56</td>
<td>3mg</td>
</tr>
<tr>
<td>21/01/2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.06</td>
<td>3mg</td>
</tr>
<tr>
<td>16/02/2007</td>
<td>2.11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3mg</td>
<td></td>
</tr>
<tr>
<td>15/03/2007</td>
<td>1.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>increase in physical activity, current weekly dose is 21mg, increase 5% to 22mg/week.</td>
<td>3mg (M-F) 3.5mg (S&amp;S)</td>
</tr>
<tr>
<td>21/03/2007</td>
<td>1.83</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>what are you going to do in this case?</td>
<td>3/52</td>
</tr>
</tbody>
</table>
Example 7: maintenance dosing

<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
<th>X</th>
<th>X</th>
<th>X</th>
<th>X</th>
<th>X</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>16/02/2007</td>
<td>2.11</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>3mg OM</td>
</tr>
<tr>
<td>15/03/2007</td>
<td>1.7</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>increase in physical activity, current weekly dose is 21mg, increase 5% to 22mg/week. 3mg (M-F) 3.5mg (S&amp;S) 3/52</td>
</tr>
<tr>
<td>21/03/2007</td>
<td>1.83</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Patient done this test in another clinic, NHC. Previous dose change is only 5-6 days ago. Any dose change, the stabilise effect could only be seen at least after 10 days. No dose change for today's visit keep the previous dose, TCU ACC 2 weeks later.</td>
</tr>
</tbody>
</table>

INR

IN R (No U O M)
**Example 8: maintenance**

<table>
<thead>
<tr>
<th>Name</th>
<th>FYM</th>
<th>DOB</th>
<th>27/06/1924</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Age</td>
<td>82</td>
</tr>
<tr>
<td>Ethnic Gp</td>
<td>Chinese</td>
<td>Indication</td>
<td>AF</td>
</tr>
<tr>
<td>I/C</td>
<td>Target INR</td>
<td>2 to 2.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duration</td>
<td>Lifelong</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Visit Date</th>
<th>Target INR</th>
<th>Bleeding</th>
<th>Thrombosis</th>
<th>New/change in meds/diet</th>
<th>New/Recent illness</th>
<th>Non-compliance</th>
<th>Notes</th>
<th>Warfarin dose</th>
<th>TCU</th>
</tr>
</thead>
<tbody>
<tr>
<td>31/10/2006</td>
<td>1.85</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Good compliance. No bleeding. No numbness. Claims that appetite lately not so good.</td>
<td>1.5mg / 2mg EOM</td>
<td>6/52</td>
</tr>
<tr>
<td>12/12/2006</td>
<td>2.10</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Y</td>
<td>No bleeding. No SOB, forgot to take 1 dose last week. Patient take medicine herself, sometimes the maid will remind her if forget.</td>
<td>?</td>
<td></td>
</tr>
</tbody>
</table>
Case 1, Newly initiated on warfarin

- 76 year old patient with PMH of: DM, HTN, CKD, Gout, PUD, TKR
- Newly diagnosed R LL DVT in Feb ‘12 – started warfarin on 06/02/12
- HAS-BLED score= 4 (high risk of bleeding)
- Case 1: 76 year old patient with PMH of: DM, HTN, CKD, Gout, PUD, TKR
- Newly diagnosed R LL DVT in Feb ‘12 – started warfarin on 06/02/12
- HAS-BLED score= 4 (high risk of bleeding)

<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
<th>Warfarin Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>06/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>07/02/2012</td>
<td>1.03</td>
<td>5</td>
</tr>
<tr>
<td>08/02/2012</td>
<td>1.12</td>
<td>7</td>
</tr>
<tr>
<td>09/02/2012</td>
<td>1.71</td>
<td>7</td>
</tr>
<tr>
<td>10/02/2012</td>
<td>2.98</td>
<td>5 (discharge)</td>
</tr>
<tr>
<td>11/02/2012</td>
<td>5</td>
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<tr>
<td>12/02/2012</td>
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<td></td>
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<tr>
<td>16/02/2012</td>
<td>5</td>
<td></td>
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<tr>
<td>17/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>18/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>19/02/2012</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>20/02/2012</td>
<td>9.27</td>
<td>f/u at Outpatient</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
<th>Warfarin Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/02/2012</td>
<td>9.27</td>
<td>? 3</td>
</tr>
<tr>
<td>21/02/2012</td>
<td>?</td>
<td>3</td>
</tr>
<tr>
<td>22/02/2012</td>
<td>?</td>
<td>3</td>
</tr>
<tr>
<td>23/02/2012</td>
<td>?</td>
<td>3</td>
</tr>
<tr>
<td>24/02/2012</td>
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<td>25/02/2012</td>
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</tr>
<tr>
<td>26/02/2012</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>27/02/2012</td>
<td>3.4</td>
<td>3</td>
</tr>
<tr>
<td>28/02/2012</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>29/02/2012</td>
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<td></td>
</tr>
<tr>
<td>01/03/2012</td>
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<td>2</td>
<td></td>
</tr>
<tr>
<td>05/03/2012</td>
<td>3</td>
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<tr>
<td>06/03/2012</td>
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</tr>
<tr>
<td>07/03/2012</td>
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<td></td>
</tr>
<tr>
<td>08/03/2012</td>
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<td></td>
</tr>
<tr>
<td>09/03/2012, 10pm</td>
<td>&gt; 10 @ A&amp;E</td>
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</tr>
<tr>
<td>10/03/2012, 10am</td>
<td>&gt;10</td>
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</tr>
<tr>
<td>09/03/2012, 9pm</td>
<td>&gt;10</td>
<td></td>
</tr>
</tbody>
</table>
Relevant problems:

• Inappropriate warfarin initiation dose:
  - Started on higher dose than suggested for patients age > 70

• Patient discharge on 10/02/12 with INR of 2.98 at upper therapeutic limit &
given relatively long TCU date of 10 days (i.e. on 20/02/12)

---

**Date** | **INR** | **Warfarin Dose (mg)**
---|---|---
06/02/2012 | 5 | 5
07/02/2012 | 1.03 | 5
08/02/2012 | 1.12 | 7
09/02/2012 | 1.71 | 7
10/02/2012 | 2.98 | 5
11/02/2012 | 5 | 5
12/02/2012 | 5 | 5
13/02/2012 | 5 | 5
14/02/2012 | 5 | 5
15/02/2012 | 5 | 5
16/02/2012 | 5 | 5
17/02/2012 | 5 | 5
18/02/2012 | 5 | 5
19/02/2012 | 5 | 5
20/02/2012 | 9.27 | 5

---

**76 year old patient with PMH of: DM, HTN, CKD, Gout, PUD, TKR**

• Newly diagnosed R LL DVT in Feb '12 – started warfarin on 06/02/12

• HAS-BLED score = 4 (high risk of bleeding)
<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
<th>Warfarin Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/02/2012</td>
<td>9.27</td>
<td>3</td>
</tr>
<tr>
<td>21/02/2012</td>
<td>?</td>
<td>3</td>
</tr>
<tr>
<td>22/02/2012</td>
<td>?</td>
<td>3</td>
</tr>
<tr>
<td>23/02/2012</td>
<td>?</td>
<td>3</td>
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<tr>
<td>24/02/2012</td>
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<td>25/02/2012</td>
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<td>26/02/2012</td>
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<tr>
<td>27/02/2012</td>
<td>3.4</td>
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<td>28/02/2012</td>
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<td>29/02/2012</td>
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<td>01/03/2012</td>
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<td>06/03/2012</td>
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<tr>
<td>08/03/2012</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>09/03/2012</td>
<td>&gt;10 @ A&amp;E</td>
<td></td>
</tr>
</tbody>
</table>

Note: Patient’s INR always supra-therapeutic since started on warfarin

• 76 year old patient with PMH of: DM, HTN, CKD, Gout, PUD, TKR
• Newly diagnosed R LL DVT in Feb ’12 – started warfarin on 06/02/12
• HAS-BLED score= 4 (high risk of bleeding)

40% weekly dose reduction & TCU in a week
?vit K given (wasn’t documented on system)

~9.5% weekly dose reduction
Patient admitted at A&E on 09/03/12 for cellulitis & over-Anticoagulation

<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/03/2012</td>
<td>&gt;10 (10pm)</td>
</tr>
<tr>
<td>10/03/2012</td>
<td>&gt;10 (10am)</td>
</tr>
<tr>
<td>10/03/2012</td>
<td>&gt;10 (9pm)</td>
</tr>
</tbody>
</table>

Relevant problems:
- Vitamin K not given when INR>10 (First INR)
- PO 3mg Vitamin K given on 10/03/12 @2.30pm (after 2nd INR reading of >10)
- INR not checked at close interval, ie 6 hours after giving vitamin K

七十六歲老年患者，有病史：2型糖尿病、高血压、慢性肾脏病、痛风、溃疡性结肠炎、TKR

新诊断右下肢DVT於2012年2月 — 开始华法林于6/02/12

HAS-BLED score= 4（高出血风险）

- @10PM, Vit K given? No documentation
- @2.30pm: PO Vit K 3mg

- @8pm: Patient unresponsive
- @9pm: INR still >10
- @11pm: IV Vit K 10mg
- @1am: Patient passed away likely due to massive ICH

管理过抗凝

无显著出血和低出血风险

- INR 4-5：华法林和检查INR 24小时后
- INR 5-9：省略下一次1-2剂量，检查INR 24小时。或给华法林1-3mg PO
- INR >9：华法林和给维他命K 3-5mg PO
- 重复检查INR 6小时后，每日3天

— 半衰期维他命K比华法林短，进一步剂量可能需要INR仍高

严重出血

- INR >1.5：华法林和给维他命K 5-10mg IV
- 鲜冷冰冻血浆 -10ml/kg
- 重复检查INR 6小时后，每日3天
- 与血科医生讨论，根据使用凝血酶原复合物的安排
### Classes of Drugs

<table>
<thead>
<tr>
<th><strong>Classe of Drugs</strong></th>
<th><strong>Examples</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensives</td>
<td>Acebutolol, Atenolol, Metoprolol</td>
</tr>
<tr>
<td>Antimicrobial Agents</td>
<td>Penicillins, Cephalosporins, Fluoroquinolones</td>
</tr>
<tr>
<td>Antineoplastics</td>
<td>Taxanes, Imatinib</td>
</tr>
<tr>
<td>Antiparasitic/Antimicrobial</td>
<td>Ivermectin, Azithromycin</td>
</tr>
<tr>
<td>Antihyperlipidemics</td>
<td>Statins, Ezetimibe</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Cetirizine, Diphenhydramine</td>
</tr>
<tr>
<td>Antineoplastic Agents</td>
<td>Taxans, Tyrosine Kinase Inhibitors</td>
</tr>
<tr>
<td>Antineoplastic Drugs</td>
<td>Paclitaxel, Carboplatin</td>
</tr>
<tr>
<td>Antitubercular Agents</td>
<td>Isoniazid, Rifampin</td>
</tr>
<tr>
<td>Antithyroid Drugs</td>
<td>Carbimazole, Methimazole</td>
</tr>
<tr>
<td>Antineoplastic Drugs</td>
<td>Mitomycin C, Cyclophosphamide</td>
</tr>
<tr>
<td>Antineoplastic Agents</td>
<td>Vinca Alkaloids, Platinum complexes</td>
</tr>
<tr>
<td>Antineoplastic Drugs</td>
<td>Gemcitabine, Paclitaxel</td>
</tr>
<tr>
<td>Antineoplastic Agents</td>
<td>Bortezomib, Lenalidomide</td>
</tr>
</tbody>
</table>

### Specific Drugs Reported

<table>
<thead>
<tr>
<th><strong>Specific Drugs</strong></th>
<th><strong>Examples</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensives</td>
<td>Amlodipine, Lisinopril, Hydrochlorothiazide</td>
</tr>
<tr>
<td>Antimicrobial Agents</td>
<td>Cefuroxime, Amoxicillin, Vancomycin</td>
</tr>
<tr>
<td>Antineoplastic Agents</td>
<td>Vinca Alkaloids, Platinum complexes</td>
</tr>
<tr>
<td>Antineoplastic Drugs</td>
<td>Mitomycin C, Cyclophosphamide</td>
</tr>
<tr>
<td>Antineoplastic Agents</td>
<td>Bortezomib, Lenalidomide</td>
</tr>
<tr>
<td>Antineoplastic Drugs</td>
<td>Gemcitabine, Paclitaxel</td>
</tr>
<tr>
<td>Antineoplastic Agents</td>
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</tr>
<tr>
<td>Antineoplastic Drugs</td>
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<tr>
<td>Antineoplastic Agents</td>
<td>Bortezomib, Lenalidomide</td>
</tr>
<tr>
<td>Antineoplastic Drugs</td>
<td>Gemcitabine, Paclitaxel</td>
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<tr>
<td>Antineoplastic Agents</td>
<td>Bortezomib, Lenalidomide</td>
</tr>
<tr>
<td>Antineoplastic Drugs</td>
<td>Mitomycin C, Cyclophosphamide</td>
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<tr>
<td>Antineoplastic Agents</td>
<td>Bortezomib, Lenalidomide</td>
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<tr>
<td>Antineoplastic Drugs</td>
<td>Gemcitabine, Paclitaxel</td>
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<tr>
<td>DRUG/AGENT NAME</td>
<td>SPECIFIC DRUGS REPORTED</td>
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<td>Acetaminophen</td>
<td>Oxycontin</td>
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<tr>
<td>Acyclovir</td>
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<td>Adequan</td>
<td>Oxycodone</td>
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<td>Oxynorm</td>
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<td>Aminosalicylic</td>
<td>Paracetaol</td>
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<td>Amlodipine</td>
<td>Paroxetine</td>
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<tr>
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<td>Penicillin</td>
</tr>
<tr>
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<td>Ampicillin</td>
<td>Perphenazine</td>
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<td>Persantine</td>
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<td>Anastrozole</td>
<td>Phenazopyridine</td>
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<td>Phenylbutazone</td>
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<td>Anagrelide</td>
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<td>Pethidine</td>
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<td>Atropine</td>
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<td>Bupivacaine</td>
<td>Prazosin</td>
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<tr>
<td>Busulfan</td>
<td>Procainamide</td>
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<td>Butazone</td>
<td>Procardia</td>
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<td>Captopril</td>
<td>Progesic</td>
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<td>Cimetidine</td>
<td>Prothrombin</td>
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<td>Coxibs</td>
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<td>Diphenhydramine</td>
<td>Tetracycline</td>
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<td>Diphenhydramine</td>
<td>Thyroid</td>
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<td>Diphenhydramine</td>
<td>Ticlopidine</td>
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<td>Diphenhydramine</td>
<td>Tissue Plasminogen Activator (t-PA)</td>
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<td>Diphenhydramine</td>
<td>Tramadol</td>
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<td>Diphenhydramine</td>
<td>Tranosol</td>
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<td>Tramadol</td>
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<td>Unaenol</td>
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<td>Diphenhydramine</td>
<td>Valproate</td>
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<td>Diphenhydramine</td>
<td>Vitamin C (high dose)</td>
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<td>Diphenhydramine</td>
<td>Vitamin K</td>
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<tr>
<td>Disease</td>
<td>Ongoing</td>
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<td>---------</td>
</tr>
<tr>
<td>• Blood dyscrasias (see contraindications)</td>
<td>• Cancer</td>
</tr>
<tr>
<td>• Cancer</td>
<td>• Collagen vascular disease</td>
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<tr>
<td>• Congestive heart failure (CHF)</td>
<td>• Diarrhea</td>
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<td>• Diarrhea</td>
<td>• Diet high in Vitamin K</td>
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<tr>
<td>• Dietary deficiencies</td>
<td>• Edema</td>
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<tr>
<td>• Elevated temperature</td>
<td>• Hepatic disorders:</td>
</tr>
<tr>
<td></td>
<td>• Infectious hepatitis</td>
</tr>
<tr>
<td></td>
<td>• Jaundice</td>
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<tr>
<td>• Hereditary coumarin resistance</td>
<td>• Hyperlipidemia</td>
</tr>
<tr>
<td>• Hyperlipidemia</td>
<td>• Hyperthyroidism</td>
</tr>
<tr>
<td>• Hyperthyroidism</td>
<td>• Nephrotic syndrome</td>
</tr>
<tr>
<td>• Other medications affecting blood elements that may modify hemostasis</td>
<td>• Poor nutritional state</td>
</tr>
<tr>
<td>• Poor nutritional state</td>
<td>• Prolonged hot weather</td>
</tr>
<tr>
<td>• Prolonged hot weather</td>
<td>• Steatorrhea</td>
</tr>
<tr>
<td>• Steatorrhea</td>
<td>• Unreliable PT/INR determinations</td>
</tr>
<tr>
<td>• Unreliable PT/INR determinations</td>
<td>• Vitamin K deficiency</td>
</tr>
</tbody>
</table>

### Botanicals that contain coumarins with potential anticoagulant effects:
- *Allaia*
- Angelica (Dong Quai)
- Aniseed
- Arnica
- Asa Foetida
- Bogbean†
- Boldo
- Buchu
- Capricum?
- Cassia†
- Celery
- Chamomile (German and Roman)
- Dandelion
- Feverfew
- German Sarsaparilla
- Ginger
- Ginkgo Biloba
- Ginseng (Panax)†
- Licorice†
- Meadowsweet†
- Nettle
- Passion Flower
- Prickly Ash (Northern)
- Quassia
- Red Clover
- Sweet Clover
- Sweet Woodruff
- Tonka Beans
- Wild Carrots
- Wild Lettuce
- Parsley

### Miscellaneous botanicals with anticoagulant properties:
- Bladder Wrack (Fucox)
- Pan d'arco

### Botanicals that contain salicylate and/or have antiplatelet properties:
- Agrimony†
- Aloe Gel
- Aspen
- Black Cohosh
- Black Haw
- Bogbean†
- Cassia†
- Clove
- Dandelion
- Feverfew
- Garlic†
- Garlic (Panax)†
- Ginseng (Panax)†
- Licorice†
- Meadowsweet†
- Onion†
- Pohosanol
- Poplar
- Senega
- Tamarind
- Willow
- Wintergreen

### Botanicals with fibrinolytic properties:
- Bromelia
- Garlic†
- Garlic (Panax)†
- Inositol Nicotinate
- Capsicum?
- Ginseng (Panax)†
- Onion†

### Botanicals with coagulant properties:
- Agrimony†
- Golden Seal
- Mistletoe
- Yarrow
### Drug-Drug Interactions

Anticoagulation Clinics of North America (ACNA). Drug Interactions with Warfarin - Requiring Preventive Dosage Changes

<table>
<thead>
<tr>
<th>Effect on INR</th>
<th>Drugs</th>
<th>Reaction</th>
<th>ACNA Warfarin Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase INR</td>
<td>Co-trimoxazole (Bactrim, Septrin)</td>
<td>Generally see INRs in the 8-20 range</td>
<td>Decrease dose 20-30%</td>
</tr>
<tr>
<td></td>
<td>Fluconazole (more than one dose)</td>
<td>Have seen INRs 15-30</td>
<td>Decrease dose 30-40%</td>
</tr>
<tr>
<td></td>
<td>Amiodarone</td>
<td>Dose and time dependent INRs in the 8-20 range</td>
<td>At 2 week intervals, decrease the dose by approximately 5-10% (usually a total of 30-50% is required)</td>
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<td>Aspirin</td>
<td>INRs usually 6-10</td>
<td>Avoid or stop Aspirin and adjust dose as for any high INR</td>
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<td>Variable - not much change in patient with chronic diarrhea or UC; others INR may increase to 8-20 range</td>
<td>Decrease dose by 10% and reassess within 3-4 days</td>
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<td>Effect on INR</td>
<td>Drugs</td>
<td>Reaction</td>
<td>ACNA Warfarin Adjustment</td>
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<td>--------------</td>
<td>-------</td>
<td>----------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Decrease INR</td>
<td>Phenobarbitone</td>
<td>Dependent on number of doses taken - generally INR 1.0 -1.4</td>
<td>Increase dose by 20% for continuous use; adjust INR to upper end of range for intermittent use</td>
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<td></td>
<td>Rifampicin</td>
<td>INR = 1.0</td>
<td>Double or Triple dose</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine</td>
<td>Dependent on dose and time frame, often INR 1.0 -1.5</td>
<td>Increase dose by 30%</td>
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<tr>
<td></td>
<td>Primidone (Mysoline)</td>
<td>Dependent on dose, INR subtherapeutic to 1.0</td>
<td>Increase the dose by 10% to 40% dependent on INR response</td>
</tr>
</tbody>
</table>
The effects of fasting in Muslim patients taking warfarin

In conclusion, fasting during Ramadan significantly increases the mean INR of Muslim patients taking warfarin and the likelihood of having an INR above therapeutic targets. For patients maintained at the higher end of INR target ranges or at increased risk of bleeding, clinicians will need to be aware of this effect and consider more intensive monitoring or pre-emptive dosage adjustments should these patients choose to fast.

**Table 2** Study results: mean INR differences between study periods and percentage of time within, above and below therapeutic range

<table>
<thead>
<tr>
<th></th>
<th>Pre-Ramadan</th>
<th>Ramadan</th>
<th>Mean difference</th>
<th>P</th>
<th>Ramadan</th>
<th>Post-Ramadan</th>
<th>Mean difference</th>
<th>P</th>
<th>Pre-Ramadan</th>
<th>Post-Ramadan</th>
<th>Mean difference</th>
<th>P</th>
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<tbody>
<tr>
<td>INR Results</td>
<td>2.44 ± 0.52</td>
<td>2.67 ± 0.57</td>
<td>0.228</td>
<td>0.006</td>
<td>2.64 ± 0.57</td>
<td>2.38 ± 0.58</td>
<td>0.283</td>
<td>&lt;0.001</td>
<td>2.44 ± 0.52</td>
<td>2.38 ± 0.58</td>
<td>0.055</td>
<td>1.000</td>
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<tr>
<td>Time within range</td>
<td>80.99</td>
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<td></td>
<td></td>
<td>69.56</td>
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<td></td>
<td></td>
<td>69.87</td>
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<tr>
<td>Time above range</td>
<td>10.80</td>
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<td>29.87</td>
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<td></td>
<td></td>
<td>14.64</td>
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</tr>
<tr>
<td>Time below range</td>
<td>8.22</td>
<td></td>
<td></td>
<td></td>
<td>0.37</td>
<td></td>
<td></td>
<td></td>
<td>15.49</td>
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</table>

Data are mean ± SD unless otherwise indicated.

**Fig. 2.** Fluctuations in quality of anticoagulation across study periods.
**Warfarin Dosing: Maintenance Phase, INR target 2-3**

### Warfarin Dosage Protocol
ECU Anticoagulation Clinic. Updated 5/18/01

#### INR Goal of 2 - 3 Chronic Therapy

- **INR <2**
  - If INR 1.9 and prior INR OK then no change INR 1-2 w
  - Assess Factors 0-2 extra doses Increase by 10-15%
  - INR 1 w: if event < 4 w
    - INR 1-2 w: if event > 4 w
    - Call MD if 4 consecutive INR <2

- **INR 2-3**
  - No change INR 3-4 w (if stable)

- **INR 3.1-5**
  - If INR <=3.3 and prior INR OK then no change INR 1-2 w
  - Decrease by 5-15% INR <1 w

- **INR 5.1-9**
  - Assess Factors
  - Hold 1-2 doses Notify MD

- **INR 9.1-20**
  - Assess Factors
  - Hold Notify MD follow instructions

- **INR >20, or Bleeding Notify MD**

- **INR Goal of 2 - 3 Chronic Therapy**

- **INR Goal of 2 - 3 Chronic Therapy**

#### Notes:
- **High Bleed Risk, >=3 of:** Age>65, Hx GI bleed, Hx Stroke, or any of the following comorbidities (recent MI, hematocrit <30%, Creat >1.5mg/dl, or DM)
- **Factors for high/low INR:** unstable comorbidity, absorption, medication interaction, change in metabolism, compliance, alcohol use, lab error, patient understanding
- **Vit K injectable form can be given PO**
- **Guidelines are not intended to replace clinician’s judgement**

---

Carlos Estrada, MD, MS. (252) 816-4633
Mary Martin Hryniewicz, RN, MSN. (252) 816-3982

[slide link] c:\account\dose2.pptislide1
Warfarin Dosing: Maintenance Phase, INR target 2.5 – 3.5

Warfarin Dosage Protocol
ECU Anticoagulation Clinic. Updated 5/18/01

INR Goal of 2.5 - 3.5
Chronic Therapy

INR < 2.5
- If INR 2.4 and prior INR OK then no change INR 1-2 w
- Assess Factors: 0-2 extra doses increase by 10-15%
  INR < 1 w
- Call MD if 2 consecutive INR < 2.5
  Consider heparin

INR 2.5 - 3.5
- No change INR 3-4 w (if stable)

INR 3.6 - 5
- If INR <= 3.8 and prior INR OK then no change INR 1-2 w
- INR 1.2 w
- Decrease by 5-15% INR < 1 w

INR 5.1 - 9
- Assess Factors: Hold 1-2 doses Notify MD
- Low Bleed Risk
  No Vit K INR 1-2 days
  Follow protocol next visit

INR 9.1 - 20
- Assess Factors: Hold Notify MD follow instructions
- High Bleed Risk or other factors follow instructions
- Urgency Vit K 2-4 mg PO INR 1 day
  May repeat Vit K Follow protocol
- Urgency Vit K 2-4 mg PO INR 1 day
  May repeat Vit K Follow protocol
- Urgency Vit K 2-4 mg PO INR 1 day
  May repeat Vit K Follow protocol

INR > 20, or Bleeding
Notify MD

- High Bleed Risk, >= 3 of: Age > 65, Hx GI bleed, Hx Stroke, or any of the following comorbidities (recent MI, hematocrit <30%, Creat > 1.5mg/dl, or DM)
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Carlos Estrada, MD, MS. (252) 816-4633
Mary Martin Hrynewicz, RN, MSN. (252) 816-3982
C:\acoum\dose2.ppt\slide2
Figure 1. Daily warfarin dose, INR, and concomitant rifampin therapy over time. The x-axis represents time in relation to the patient’s clinic visit dates. The left y-axis represents the warfarin dose administered in milligrams/day and is shown by the vertical bars. The right y-axis represents INR units and is shown by the black diamond points, with the therapeutic range indicated as 2.0–3.0. The time period of concomitant rifampin administration is shown as the horizontal gray bar.
Figure 1. The patient’s weekly warfarin dose and international normalized ratios (INRs). (Note that intervals between dates are not consistent.)
Thank you!

Email: kong.ming.chai@sgh.com.sg
<table>
<thead>
<tr>
<th>Effect on INR</th>
<th>Drugs</th>
<th>Reaction</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Increase INR</td>
<td></td>
<td></td>
<td>(Always see the patient back within 3 - 4 days maximum to readjust if necessary)</td>
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<td></td>
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### Example 8: maintenance

<table>
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<th>FYM</th>
<th>DOB</th>
<th>27/06/1924</th>
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<tbody>
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<td>Sex</td>
<td>Female</td>
<td>Age</td>
<td>82</td>
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<tr>
<td>Ethnic Gp</td>
<td>Chinese</td>
<td>Indication</td>
<td>AF</td>
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<td>I/C</td>
<td>Target INR</td>
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<td></td>
<td>Duration</td>
<td>Lifelong</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Visit Date</th>
<th>Target</th>
<th>Bleeding</th>
<th>Thrombosis</th>
<th>New/change in meds/diet</th>
<th>New/Recent illness</th>
<th>Non-compliance</th>
<th>Notes</th>
<th>Warfarin dose</th>
<th>TCU</th>
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</thead>
<tbody>
<tr>
<td>31/10/2006</td>
<td>1.85</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>Good compliance. No bleeding. No numbness. Claims that appetite lately not so good.</td>
<td>1.5mg / 2mg EOM</td>
<td>6/52</td>
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<tr>
<td>12/12/2006</td>
<td>2.10</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>Y</td>
<td>No bleeding. No SOB, forgot to take 1 dose last week. Patient take medicine herself, sometimes the maid will e wind her if forget.</td>
<td>1.5mg / 2mg EOM</td>
<td>8/52</td>
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<td>06/02/2007</td>
<td>2.70</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>no smoking. No alcohol. No change in activity.</td>
<td>?</td>
<td></td>
</tr>
</tbody>
</table>
## Example 9: Maintenance

<table>
<thead>
<tr>
<th>Visit Date</th>
<th>Target</th>
<th>Bleeding</th>
<th>Thrombosis</th>
<th>New/Change in Meds/Diet</th>
<th>New/Recent Illness</th>
<th>Non-compliance</th>
<th>Notes</th>
<th>Warfarin Dose</th>
<th>TCU</th>
</tr>
</thead>
<tbody>
<tr>
<td>31/10/2006</td>
<td>1.85</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Good compliance. No bleeding. No numbness. Claims that appetite lately not so good.</td>
<td>1.5mg / 2mg EOM</td>
<td>6/52</td>
</tr>
<tr>
<td>12/12/2006</td>
<td>2.10</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Y</td>
<td></td>
<td>No bleeding. No SOB, forgot to take 1 dose last week. Patient take medicine herself, sometimes the maid will remind her if forget.</td>
<td>1.5mg / 2mg EOM</td>
<td>8/52</td>
</tr>
<tr>
<td>06/02/2007</td>
<td>2.70</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>No smoking. No alcohol. No change in activity. INR on rising trend. Currently on 12.5mg/week. Reduce weekly dose by 8% to 11.5mg/week</td>
<td>1.5 mg (Mon - Fri), 2mg (Sat &amp; Sun)</td>
<td>6/52</td>
</tr>
<tr>
<td>20/03/2007</td>
<td>2.40</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>c/o of diarrhea for 5/7. Not taking any medicine. No smoking, no alcohol, no change in activity. C/o of leg swelling after prolonged walking, apply Bengay for the pain. Took Brand chicken essence</td>
<td>?</td>
<td></td>
</tr>
</tbody>
</table>
Example 9: maintenance

<table>
<thead>
<tr>
<th>Visit Date</th>
<th>Target</th>
<th>Bleeding</th>
<th>Thrombosis</th>
<th>New in meds/diet</th>
<th>Non-compliance</th>
<th>Notes</th>
<th>Warfarin dose</th>
<th>TCU</th>
</tr>
</thead>
<tbody>
<tr>
<td>31/10/2006</td>
<td>2.0 to 2.5</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Good compliance. No bleeding. No numbness. Claims that appetite lately not so good.</td>
<td>1.5mg / 2mg EOM</td>
<td>6/52</td>
</tr>
<tr>
<td>12/12/2006</td>
<td>2.10</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>Y</td>
<td>No bleeding. No SOB, forgot to take 1 dose last week. Patient take medicine herself, sometimes the maid will ewmind her if forget.</td>
<td>1.5mg / 2mg EOM</td>
<td>8/52</td>
</tr>
<tr>
<td>06/02/2007</td>
<td>2.70</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>no smoking. No alcohol. No change in activity. INR on rising trend. Currently on 12.5mg/week. Reduce weekly dose by 8%.</td>
<td>1.5 mg (Mon - Fri), 2mg (Sat &amp;Sun)</td>
<td>6/52</td>
</tr>
<tr>
<td>20/03/2007</td>
<td>2.40</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>c/o of diarrhea for 5/7. Not taking any medicine. No. smoking, no alcohol, no change in activity. C/o of leg swelling after prolonged walking, apply Bengay for the pain. Took Brand chicken essence</td>
<td>1.5 mg (Mon - Fri), 2mg (Sat &amp;Sun)</td>
<td>2/12</td>
</tr>
</tbody>
</table>

Diarrhea may cause increase in INR, because no Vit K synthesis from gut microflora
Example 10.1

- Mr Bram DG, 65 yo Male, Eurasian.
- Indication for Warfarin: Chronic AF with CVA,
- Target INR: 2-3
- Duration: long term
- 1st visit on 6/1/2009: INR = 2.4
- No sign and symptoms of bleeding
- No sign and symptoms of thrombosis
- No change in diet, good appetite
- No change in medications
- No recent illness, eg no cough & cold, no pain, not taking any Abx or painkiller
- Compliance with medicine
- Plan: Keep to current dose 49mg/week, ie 7mg om x 8/52
Example 10.2

- Mr Bram DG, 65 yo Male, Eurasian.
- Indication for Warfarin: Chronic AF with CVA,
- Target INR: 2-3
- Duration: long term

- 2nd visit on 7/2/2009: INR = 2.63
- 1st visit on 6/1/2009: INR = 2.4
- Patient was warded,
  - new onset R sided facial pain, UL pain x 1/7
  - new slurring of speech, deviation of mouth to L side
  - no chest pain palpitation SOB giddiness loss of vision dysphagia
  - no new onset facial weakness or sensory loss
  - alert conscious GCS 15 oriented T/P/P slurred speech
Example 10.3

- Mr Bram DG, 65 yo Male, Eurasian.
- Indication for Warfarin: Chronic AF with CVA,
- Target INR: 2-3  
  Duration: long term
- 2nd visit on 7/2/2009: INR = 2.63
- 1st visit on 6/1/2009: INR = 2.4

- Conclusion:
  1. Chronic infarcts of the brain in the vascular territories of the left ACA (anterior Cerebral Artery) and MCA (middle cerebral artery) with encephalomalacia and gliosis.
  2. Old infarcts are also noted in the right cerebellum.
  3. No acute infarct is detected.
  4. NSEMI, on 10/2/09 pt had chest pain cardiac enzyme was elevated with some new ECG changes ST depression V3 - V6 T inversion V3-V6.

- Ref to Cardiology team to r/v the pt. Impression was NSEMI and started on aspirin asked to continue current medications and gave TCU date to see Cardiologist in 6/52 to consider further investigations and treatments
Example 10.4

- Mr Bram DG, 65 yo Male, Eurasian.
- Indication for Warfarin: Chronic AF with CVA,
- Target INR: 2-3
- Duration: long term
- 2nd visit on 7/2/2009: INR = 2.63
- 1st visit on 6/1/2009: INR = 2.4

- Discharge with:
- Warfarin 7mg OM,
- Gabapentin 300mg bd, Metformin, Phenytoin, telmisartan, ISMN, omeprazole

- Started:
- Aspirin 100mg OM
- Bisoprolol 1.25mg OM
- Trimetazidine 20mg TDS,
- GTN prn,
- Tramadol 50mg TDS
- TCU Cardiologist 6/52, ACC 1/52
Example 10.5: Questions

- Patient was on warfarin for AF with history of stroke
- Now that patient had another stroke at INR of 2.63 (Target 2-3)
- According to ACCP guideline: either
  - A) Increase the target range to 2.5-3.5 or
  - B) To add ASPIRIN and maintain same range 2-3
Example 10.6 - Questions

- Patient was on warfarin for AF with history of stroke
- Now that patient had another stroke at INR of 2.63 (Target 2-3)
- According to ACCP guideline: either
  - A) Increase the target range to 2.5-3.5 or
  - B) To add ASPIRIN and maintain same range 2-3

- Cardiologist decided to add on ASPIRIN 100mg OM
- Instead of increase the target INR to 2.5 – 3.5,
  - because (Aspirin + Warfarin) → higher risk of bleeding,
- Patient newly discharge will need closer monitoring,
- Therefore TCU ACC x 1/52
Example 10.7 - Mr Bram DG, 65 yo Male, Eurasian. Chronic AF, recurrent CVA, Target INR : 2-3 Duration: long term

- 3rd visit on 19/2/2009 : INR = 3.1 (target 2-3), one week after discharge
- No sign and symptoms of bleeding
- Recent stroke, discharge from hospital 1/52 ago, (thrombosis)
- No change in diet, good appetite
- Change in medicine, newly added Aspirin 100mg OM, Bisoprolol 1.25mg OM
- Trimetazidine 20mg TDS, GTN prn.
- c/o Right facial muscle tension, c/o Right leg pain and tension in the left leg.
- Doctor increase Gabapentin dose from 300mg bd to 300mg tds
- No smoking, No Alcohol, No change in activity.
- Compliance with medicine
- Currently Warfarin weekly dose 49mg/wk.
- INR today 3.1 (Target INR 2-3)
Example 10.8 - Mr Bram DG, 65 yo Male, Eurasian. Chronic AF, recurrent CVA, Target INR : 2-3 Duration: long term

- 3rd visit on 19/2/2009 : INR = 3.1
- No sign and symptoms of bleeding
- Recent stroke, discharge from hospital 1/52 ago, (thrombosis)
- No change in diet, good appetite
- Change in medicine, newly added Aspirin 100mg OM, Bisoprolol 1.25mg OM
- Trimetazidine 20mg TDS, GTN prn.
- c/o Right facial muscle tension, c/o Right leg pain and tension in the left leg.
- Doctor increase Gabapentin dose from 300mg bd to 300mg tds
- No smoking, No Alcohol, No change in activity. Compliance with medicine

• Currently Warfarin weekly dose 49mg/wk. INR today 3.1 (Target INR 2-3)

• Should we adjust the warfarin dose?
• Patient is currently on aspirin and warfarin
• Patient is 65 yo, with recent stroke
• A) Keep the same dose, warfarin 7mg OM and tcu 1-2/52 ?
• B) Reduce the dose and tcu 1-2/52?
Example 10.9 - Mr Bram DG, 65 yo Male, Eurasian. Chronic AF, recurrent CVA, Target INR : 2-3 Duration: long term

- 3rd visit on 19/2/2009 : INR = 3.1
- No sign and symptoms of bleeding
- Recent stroke, discharge from hospital 1/52 ago, (thrombosis)
- No change in diet, good appetite
- Change in medicine, newly added Aspirin 100mg OM, Bisoprolol 1.25mg OM
- Trimetazidine 20mg TDS, GTN prn.
- c/o Right facial muscle tension, c/o Right leg pain and tension in the left leg.
- Doctor increase Gabapentin dose from 300mg bd to 300mg tds
- No smoking, No Alcohol, No change in activity. Compliance with medicine

• Current Warfarin (7mg OM) wkly dose 49mg/wk.

• INR today 3.1 (Target INR 2-3)

• Previous INR,
  - 6/1/2009 : INR = 2.4
  - 7/2/2009 : INR = 2.63 (warded for CVA, aspirin 100mg om added 1/52 ago)
  - 19/2/2009 : INR = 3.1

• How would you dose today?
Example 8.10 - Mr Bram DG, 65 yo Male, Eurasian. Chronic AF, recurrent CVA, Target INR : 2-3 Duration: long term

3rd visit on 19/2/2009 : INR = 3.1
No sign and symptoms of bleeding
Recent stroke, discharge from hospital 1/52 ago, (thrombosis)
No change in diet, good appetite
Change in medicine, newly added Aspirin 100mg OM, Bisoprolol 1.25mg OM
Trimetazidine  20mg TDS, GTN prn.
c/o Right facial muscle tension, c/o Right leg pain and tension in the left leg.
Doctor increase Gabapentin dose from 300mg bd to 300mg tds
No smoking, No Alcohol, No change in activity. Compliance with medicine
Currently Warfarin weekly dose 49mg/wk. INR today 3.1 (Target INR 2-3)
Previous INR,
- 6/1/2009 : INR = 2.4
- 7/2/2009 : INR = 2.63 (warded for CVA, aspirin 100mg om added 1/52 ago)
- 19/2/2009 : INR = 3.1

Stop warfarin for 2/7
Example 10.11 - Mr Bram DG, 65 yo Male, Eurasian. Chronic AF, recurrent CVA, Target INR : 2-3 Duration: long term

1. Why stop 2 days?

- Stop 1 day, INR would reduce by 0.3 to 0.5
- Using INR : -0.3/day as a gauge, reduce 2 days would bring the INR from 3.1 \( \rightarrow \) 2.8 \( \rightarrow \) 2.5

How much to reduce the warfarin dose?
Example 10.12 - Mr Bram DG, 65 yo Male, Eurasian. Chronic AF, recurrent CVA, Target INR: 2-3 Duration: long term

- Current Warfarin weekly dose 49mg/wk or 7mg OM
- INR today 3.1 (Target INR 2-3)

- How much to adjust?
  - 2.5 (Target INR) – 3.1 (today) = - 0.6
  - ie to decrease warfarin wkly dose by 6%, ie from 49 mg/wk to 46.06 mg/wk
  - rounded to 46mg/week ie
  - Warfarin 7mg (Mon to Thu) am, 6mg (Fri – Sun) am x 19/7
  - Always check with patient on the regime whether they can remember or not.
  - Make it convenient for them!!

- When is the next TCU?
Example 10.13  Mr Bram DG, 65 yo Male, Eurasian. Chronic AF, recurrent CVA, Target INR : 2-3 Duration: long term

- Currently Warfarin weekly dose 49mg/wk. INR today 3.1 (Target INR 2-3)
- Plan : To ↓ 6% to 46mg/wk ie
- Stop warfarin for 2/7, then
  - { Warfarin 7mg (Mon to Thu) am, 6mg (Fri – Sun) am } x 19/7

3. TCU 19/7? (close to 3/52)

Warfarin $T_{1/2}$ 20-60 hours, average 40 hours,

Prothrombin $T_{1/2} = 60$ hours

To reach a new steady state, takes about 5 $T_{1/2}$

ie depend on the longest $T_{1/2}$, ie prothrombin $T_{1/2} = 60$ hours

5 x 60 hours = 300 hours ie 12.5 days

Therefore, the new steady state will take about 2 weeks to achieve.

In this case, we gave extra 1 week, ie total 3 weeks to reach the new steady state
Example 10.14 - Mr Bram DG, 65 yo Male, Eurasian. Chronic AF, recurrent CVA, Target INR : 2-3 Duration: long term

- 3rd visit on 19/2/2009: INR = 3.1
- No sign and symptoms of bleeding
- Recent stroke, discharge from hospital 1/52 ago, (thrombosis)
- No change in diet, good appetite
- Change in medicine, newly added Aspirin 100mg OM, Bisoprolol 1.25mg OM
- Trimetazidine 20mg TDS, GTN prn.
- c/o Right facial muscle tension, c/o Right leg pain and tension in the left leg.
- Doctor increase Gabapenten dose from 300mg bd to 300mg tds
- No smoking, No Alcohol, No change in activity, Compliance with medicine
- Currently Warfarin weekly dose 49mg/wk. INR today 3.1 (Target INR 2-3)
- Previous INR,
  - 6/1/2009 : INR = 2.4
  - 7/2/2009 : INR = 2.63 (warded for CVA, aspirin 100mg om added 1/52 ago)
  - 19/2/2009 : INR = 3.1

- Stop warfarin for 2/7,
- Decrease warfarin wkly dose by 6%, ie from 49 mg/wk to 46mg/wk
- Warfarin 7mg (Mon to Thu) am, 6mg (Fri – Sun) am  x 19/7
Example 10.15

- Mr Bram DG, 65 yo Male, Eurasian.
- Indication for Warfarin: Chronic AF with CVA,
- Target INR: 2-3
- Duration: long term

4th visit on 10/3/2009: INR = 2.5

- No sign and symptoms of bleeding
- No sign and symptoms of thrombosis
- No change in diet, good appetite
- No change in medications
- No recent illness, eg no cough & cold, no pain, not taking any Abx or painkiller
- Compliance with medicine

Plan: Keep to current dose 46mg/week, ie 7mg (Mon-Thu), 6mg (Fri-Sun) x 4/52
Example 10.16

- Mr Bram DG, 65 yo Male, Eurasian.
- Indication for Warfarin: Chronic AF with CVA,
- Target INR: 2-3 Duration: long term

- 5th visit on 7/4/2009: INR = 2.4

- No sign and symptoms of bleeding
- No sign and symptoms of thrombosis
- No change in diet, good appetite
- No change in medications
- No recent illness, eg no cough & cold, no pain, not taking any Abx or painkiller
- Compliance with medicine

- Plan: Keep to current dose 46mg/week, i.e. 7mg (Mon-Thu), 6mg (Fri-Sun) x 4/52
Thank you!

Email: kong.ming.chai@sgh.com.sg