QUALITY IMPROVEMENT & BENCHMARKING

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Disclosures

- I have no financial conflict of interest related to this talk
Optimizing AC Therapy

- Provider with specific knowledge and skill
- Organized system of follow up
- Access to accurate laboratory results
- Functional communication & education system
- www.excellence.acforum.org
Types of Quality Measures

- Outcomes (INR results, thromboembolism, major bleeding, death)
- Processes (Choosing an anticoagulant, DOAC dose selection, warfarin dose adjustment, INR recall interval)
- Structures (workload statistics, organizational structure)

Definitive Outcomes

- Major bleeding, TE, and death are definitive outcomes of anticoagulation therapy
- Occur infrequently
- Lack of widely accepted standardized definitions
  - Major bleeding
  - Clinically-relevant non-major bleeding
  - Bleeding resulting in hospitalization/ED visit
- Do not always follow poor management
Reporting Methodology

<table>
<thead>
<tr>
<th>Method</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self reporting</td>
<td>Subject to under reporting</td>
</tr>
<tr>
<td>Administrative data query</td>
<td>Efficient but false positives common</td>
</tr>
<tr>
<td>Medical record review</td>
<td>Time intensive &amp; impractical for routine use</td>
</tr>
</tbody>
</table>

For identifying ADRs through administrative data queries:
- Bleeding ICD-9 codes appear to have acceptable PPV (in this study)
- Thromboembolism ICD-9 codes did not perform well

<table>
<thead>
<tr>
<th>Description</th>
<th>Number of definite bleeds/clots</th>
<th>Number of charts</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial bleeds</td>
<td>73</td>
<td>78</td>
<td>94% (86–97)</td>
</tr>
<tr>
<td>GI bleeds</td>
<td>142</td>
<td>158</td>
<td>90% (84–94)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>29</td>
<td>35</td>
<td>83% (67–92)</td>
</tr>
<tr>
<td>Vaginal bleeding</td>
<td>47</td>
<td>49</td>
<td>96% (86–99)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>17</td>
<td>18</td>
<td>94% (74–99)</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>15</td>
<td>16</td>
<td>94% (72–99)</td>
</tr>
<tr>
<td>Hemorrhage NOS</td>
<td>6</td>
<td>7</td>
<td>86% (49–97)</td>
</tr>
<tr>
<td>Joint bleed NOS</td>
<td>0</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Pericardial bleed NOS</td>
<td>0</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Definite bleed totals</strong></td>
<td><strong>329</strong></td>
<td><strong>361</strong></td>
<td><strong>91% (88–94)</strong></td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>102</td>
<td>179</td>
<td>57% (50–64)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>17</td>
<td>26</td>
<td>65% (46–81)</td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td>64</td>
<td>86</td>
<td>74% (64–82)</td>
</tr>
<tr>
<td><strong>Thromboembolism totals</strong></td>
<td><strong>183</strong></td>
<td><strong>291</strong></td>
<td><strong>63% (57–68)</strong></td>
</tr>
</tbody>
</table>
ADR Reporting

- Self-reporting might be improved by a systematic process (e.g. ask with every INR/Patient contact)
- Selective use of ICD-9/10 codes (e.g. ICH, GIB)
- Identify potential ADRs with ICD-9/10 codes & confirm with chart review
- Natural language processing
- Combined methods
Final Thoughts on ADR Monitoring

- Recognized difficulties
- Not all ADRs are the result of inadequate anticoagulation therapy management
  - Surrogate outcomes more consistent with quality?
- Internal tracking using consistent methodology is worthwhile
- Identification of QI opportunities
- Comparison to external benchmarks with due caution

Surrogate Outcome Measures

- An ideal surrogate outcome measure would:
  - Occur commonly
  - Be easy to calculate
  - Account for the underlying characteristics of the measured population
  - Be convincingly linked to definitive outcomes
TTR: Linear Interpolation (Rosendaal Method)

- Difficult to calculate
- Many variations
- Requires at least two INRs
- Has been linked to outcomes (bleeding, TE)

\[
\text{TTR} = 60\%
\]

How Well Does TTR Predict ADRs?

<table>
<thead>
<tr>
<th>TTR Quintile</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>1.0</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Good</td>
<td>1.36</td>
<td>0.7 - 2.6</td>
<td>0.34</td>
</tr>
<tr>
<td>Average</td>
<td>1.44</td>
<td>0.8 - 2.6</td>
<td>0.21</td>
</tr>
<tr>
<td>Below average</td>
<td>2.11</td>
<td>1.3 - 3.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Poor</td>
<td>1.9</td>
<td>1.1 - 3.2</td>
<td>0.02</td>
</tr>
</tbody>
</table>

C-statistic = 0.59
TTR: Comparing Apples to Apples?

- Exact vs. expanded INR range?
- Should INRs during initiation, hospitalizations and therapy interruptions be included?
- Average of TTR for each patient vs. total TTR/total days on treatment for entire clinic?
- Linear interpolation methodology?
  - Rounding estimated INR
  - Daily estimated INRs vs. continuous time
- Risk-adjusted TTR?
For CHADS<sub>2</sub> of 2 or more:
  - Only those with TTR >70% experienced fewer strokes compared to no warfarin

For all patients with AF:
  - Those with TTR <40% had MORE strokes

INR Variability (Fihn Variability)

- Difficult to calculate
- Has been linked to outcomes

In the 3 months prior to event (bleeding, TE, or death)

<table>
<thead>
<tr>
<th>Fihn Variability Quintile</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>1.0</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Good</td>
<td>1.32</td>
<td>0.7 - 2.6</td>
<td>0.42</td>
</tr>
<tr>
<td>Average</td>
<td>2.43</td>
<td>1.4 - 4.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Below average</td>
<td>2.20</td>
<td>1.3 - 3.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Poor</td>
<td>3.30</td>
<td>1.9 - 5.7</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

C-statistic = 0.64
Percent INRs in Therapeutic Range

- Easier to calculate
- Requires only one INR
- Is linked to outcomes (bleeding, TE)
- Can be influenced by frequency of INR measurements
Other Measures of INR Control

- Cross-section of the files
  - Easy to calculate
  - Rarely used
  - Better than nothing

- Extreme INR values
  - Utility unknown
  - Lack of agreed upon cut-off points

Should patients with varying levels of TTR (stability) be managed differently?

- Very stable
  - TTR >70%
  - Less intensive effort
  - Longer INR recall intervals
  - Automated response (IVR, email, letter)
  - Does stability predict future stability?

- Everyone else

- Very unstable
  - TTR <40%
  - Focused efforts to improve
  - Compliance
  - Review education
  - Vitamin K supplementation?
  - PSM/PST/weekly monitoring
  - Nomogram compliance
Process Measures

- Assess components of the patient encounter including timeliness of care
- Ideally, improvements in process measures can be linked to improved outcome measures
- Reasonably likely with surrogate outcome measures like INR control

Dosing Decision Support

*Variation in Warfarin Dose Adjustment Practice Is Responsible for Differences in the Quality of Anticoagulation Control Between Centers and Countries: An Analysis of Patients Receiving Warfarin in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Trial*
Harriette G.C. Van Spall, Lars Wallentin, Salim Yusuf, John W. Eikelboom, Robby Nieuwlaat, Sean Yang, Conrad Kabali, Paul A. Reilly, Michael D. Ezekowitz and Stuart J. Connolly

*Circulation. 2012;126:2309-2316; originally published online October 1, 2012;*
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adjusted Change in Mean TTR</th>
<th>95% Confidence Intervals</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient-level</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per year)</td>
<td>-0.07</td>
<td>-0.13, 0.00</td>
<td>0.0317</td>
</tr>
<tr>
<td>Weight (per kg)</td>
<td>0.03</td>
<td>0.00, 0.06</td>
<td>0.9887</td>
</tr>
<tr>
<td>Male (yes vs no)</td>
<td>1.37</td>
<td>0.30, 2.45</td>
<td>0.0121</td>
</tr>
<tr>
<td>White</td>
<td>2.27</td>
<td>0.72, 3.82</td>
<td>0.0041</td>
</tr>
<tr>
<td>Current smoker</td>
<td>-3.70</td>
<td>-5.57, -1.82</td>
<td>0.0001</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>-2.70</td>
<td>-3.81, -1.60</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>-0.99</td>
<td>-1.60, 0.81</td>
<td>0.5250</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>-1.74</td>
<td>-2.97, -0.50</td>
<td>0.0058</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>-1.11</td>
<td>-2.60, 0.38</td>
<td>0.1442</td>
</tr>
<tr>
<td>Previous warfarin use</td>
<td>3.63</td>
<td>2.63, 4.62</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current amiodarone use</td>
<td>-2.11</td>
<td>-3.66, -0.56</td>
<td>0.0077</td>
</tr>
<tr>
<td>Current insulin use</td>
<td>-2.36</td>
<td>-4.83, 0.12</td>
<td>0.0626</td>
</tr>
<tr>
<td><strong>Center-level</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Algorithm-consistent dosing (per 10%)</td>
<td>6.12</td>
<td>5.65, 6.59</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Secondary/tertiary hospital</td>
<td>0.65</td>
<td>-0.84, 2.15</td>
<td>0.3916</td>
</tr>
<tr>
<td>Anticoagulation clinic</td>
<td>1.02</td>
<td>-0.48, 2.52</td>
<td>0.1829</td>
</tr>
</tbody>
</table>

![Graph showing the relationship between mean country TTR and mean country algorithm-consistency. The graph suggests a positive correlation with R² = 0.65.](image-url)
Dosing Decision Support

- Algorithm-consistent dosing appears to be an important process measure
- Has been linked to both surrogate (TTR) and definitive (stroke and bleeding) outcomes
- Every 10% increase in algorithm-consistent dosing predicted:
  - 6.12% increase in TTR
  - 8% decrease in rate of stroke, systemic embolism or major bleeding

Gaps in INR monitoring

- Gaps >84 days negatively correlate with TTR
- Sites with more gaps per patient-year had worse anticoagulation control
- Strategies to improve gaps in monitoring may improve anticoagulation control
Prompt INR Follow Up

- Time to next INR after INRs >3.9 or <1.6 correlated negatively with TTR
- Sites with shorter mean recall intervals had better control
- Follow up within 1 week seemed to be ideal
- Strategies to optimize recall interval may improve anticoagulation control

Circ Cardiovasc Qual Outcomes. 2011;4:276-282

Targeted INR

- % of patients with mean INR near 2.5 is implicit measure of targeted INR
- Positively correlated with site-level INR control
- Avoiding non-standard INR ranges (explicitly or implicitly) may improve anticoagulation control

Structural Measures: Organization

- Patient volume
- Staffing
- Leadership
- Method of follow up
- Ideally these should be linked to outcomes if possible
  - May require comparisons to other services

Workload

- Number of patients/provider
- Number of INRs processed/day
- Time-flow studies
- Should be linked to outcomes if possible
Other Quality Improvement Efforts

- Mitigate avoidable drug interactions
  - D/C aspirin

- Verifying appropriate anticoagulation selection
  - Confirm CHA$_2$DS$_2$-VASc warrants anticoagulation

- Avoid inappropriate bridge therapy
  - Low-moderate risk patients taking warfarin
  - DOAC interruption

- Others?

What About DOACs?

- Surrogate outcomes less well defined
- Deviations from approved dosing

- Renal function
  - Baseline assessment
  - Follow-up assessments
  - Using appropriate dose based on renal function

- Compliance
  - Refill history
  - Medication possession ratio / proportion of days covered
Non-Vitamin K Anticoagulant Dose Selection

It's Best to Read and Follow the Di...n amid to those receiving warfarin therapy. The study by Steinberg et al. (3) highlights an important opportunity to improve NOAC therapy quality and outcomes. The quality of warfarin therapy management is often measured by using time spent in the therapeutic international normalized ratio range (7,8). A similar quality metric is needed for patients receiving NOACs and based on the results of this study, the proportion of patients receiving NOAC doses consistent with product labeling has potential as a metric that could be tracked by health care systems over time. Once identified, targeted interventions to correct nonapproved NOAC doses could then be implemented. A similar targeted approach has been shown to improve NOAC therapy adherence (9).

Key Points

- Efforts focused on improving anticoagulation control likely to improve outcomes:
  - Gaps in INR monitoring/Nonadherence process
  - Recall interval following out of range INRs
  - Standard INR targets
  - Follow guidelines consistently
  - Decision support
  - Dose DOACs consistent with label

- TTR benchmarking and ADR trending within systems likely helpful
Example Dashboard

Does any of this matter?

Things we worked on to increase TTR:
- Warfarin dose selection consistent with decision support
- Recheck INR 7 to 14 days after out-of-range INR
- No tamper zone (i.e. no dose change for unexplained INR 1.8-1.9, 3.1-3.2)
- Reinforced nonadherence protocols

Figure S1. Time spent in the therapeutic range [TIR] by the Rosendaal method according to twice annual benchmarking reports. All patients with target INR 2-3 managed by the Clinical Pharmacy Anticoagulation and Anemia Service at Kaiser Permanente Colorado are included. Historical data only available dating back to October 2008. Data provided by Dawn AC® (4S Systems, Cumbria UK).
Significant reductions in stroke/SE, major bleeding, and all-cause mortality.