Optimal Medical Therapy (OMT): OMG it really works!

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Chair, Foundation for Medical Education and Research

DISCLOSURE
Research grants, advisory board, speaking honoraria for:
Abbott, Actelion, AstraZeneca, Bayer, BMS, CardioComm Solutions, GSK, Johnson and Johnson, Merck, Novartis, NovoNordisc, Pfizer, Roche, Sanofi, Valeant
Pathology of Culprit Lesion

Strategies:
1. Aspirin ± 2nd agent (ACS and/or stent)
2. ACE inhibitor
3. Statin ± CAI for LDL control
4. BP Control
5. Beta blocker for LVD or CHF but not HT
6. ? Glycemic control
Discordance Between Physicians’ Estimation of Patient Cardiovascular Risk and Use of Evidence-Based Medical Therapy

Jennifer L.Y. Tsang, MD, Aurora Mendelsohn, PhD, Mary K.K. Tan, BSc, Daniel G. Hackam, MD, Lawrence A. Leiter, MD, David Fitchett, MD, Peter J. Lin, MD, Etienne Grima, BSc, Anatoly Langer, MD, MSc, and Shaun G. Goodman, MD, MSc, for the Vascular Protection Registry and Guidelines Oriented Approach to Lipid Lowering Registry Investigators

Despite clinical trial evidence supporting the use of antiplatelets, angiotensin-converting enzyme inhibitors, and statins for cardiovascular risk reduction in high-risk patients, use of such therapies in real-world outpatients in the prospective Vascular Protection Registry and the Guidelines Oriented Approach to Lipid Lowering Registry was suboptimal (78%, 55%, and 75%, respectively). The most frequent reason physicians cited for nonprescription of statins (33%) was that patients were not high risk enough and/or current guidelines did not support statin use. In conclusion, outpatients at high cardiovascular risk continue to be undertreated as a result of a combination of physician underestimation of cardiovascular risk (knowledge gap) and barriers to implementation of evidence-based therapy (practice gap). © 2008 Elsevier Inc. All rights reserved. (Am J Cardiol 2008;102:1142–1145)
Factors influencing underutilization of evidence-based therapies in women†

Raffaele Bugiardini1*, Andrew T. Yan2, Raymond T. Yan2, David Fitchett2, Anatoly Langer2, Olivia Manfrini1, and Shaun G. Goodman2, on behalf of the Canadian Acute Coronary Syndrome Registry I and II Investigators*

Methods and results
From the Canadian Registry of ACS I and II, 6558 patients (4471 men and 2087 women) with a final diagnosis of ACS were selected for the current analysis. Covariates were chosen using the approach described by Blackstone. The final selected model included 23 patient clinical variables. Women were less likely than men to receive beta-blockers (75.76 vs. 79.24%; P < 0.01), lipid-modifying agents (56.37 vs. 65.44%; P < 0.0001), and angiotensin-converting enzyme (ACE)-inhibitors (55.52 vs. 59.99%; P < 0.01). Female sex and clinical decision not to investigate with cardiac catheterization were the strongest independent predictors for not receiving lipid-modifying agents and ACE-inhibitors. Age, Killip class 2, and Killip class 3/4 were significant independent predictors of underutilization of beta-blocker use. Women were older (69 ± 12 vs. 64 ± 12; P < 0.01) with a higher prevalence of Killip class ≥ 2 (19.95 vs. 15.54%; P < 0.068), and they were less likely to be referred for cardiac catheterization (41.9 vs. 49.6%; P < 0.001).

Conclusions
The current findings demonstrate that underutilization of evidence-based therapies in women with ACS compared with men is associated with multiple factors related to the patient (age), the consequences of the disease (congestive heart failure), and the physician’s assessment of patient risk (decision to catheterize). Female gender remains associated with underutilization of lipid-modifying agents and ACE-inhibitors despite adjustment for these confounders.

Keywords
Women • Evidence-based therapies
Results: Patients with Diabetes at Goal

- A1c < 7.0%
  - Solo Physicians (n=464): 55.0%
  - MGs (n=900): 50.0%
  - P = 0.042

- BP < 130/80 mmHg
  - Solo Physicians (n=464): 50.0%
  - MGs (n=900): 50.0%
  - P = 0.463

- LDL-C < 2 mmol/L
  - Solo Physicians (n=464): 40.0%
  - MGs (n=900): 40.0%
  - P = 0.943

- All 3 Endpoints
  - Solo Physicians (n=464): 20.0%
  - MGs (n=900): 20.0%
  - P = 0.047
Estimated (CCHS 2003 data) number of events among 2.2M high risk (defined as >50 y.o. + Canadians over the next 10 years.

1.1 M

Based on VP and GOALL data

31% 143,041

609,805 466,763

Langer et al Can J Cardiol 2008;24(5):363-68.
Direct Relationship Between LDL-C Reduction and Coronary Events:
For every 1 mmol/L of LDL reduction there is 1% absolute (20% relative) reduction in CVD mortality

Each 2 mm Hg Decrease in SBP Reduces CV Risk by 7 to 10%

- Meta-analysis of 61 prospective observational studies
- 1 million adults aged 40–69 years with BP > 115/75 mm Hg
- 12.7 million person-years

**2 mm Hg decrease in mean SBP**

7% reduction in risk of IHD and other vascular disease mortality

10% reduction in risk of stroke mortality

BP Control: Choose the right agent

ACCOMPLISH: ACEI + CCB Reduced CV Events
More Than ACEI + HCTZ

ASCOT: CV death + MI + stroke

Atenolol ± thiazide
(No. of events = 937)

Amlodipine ± perindopril
(No. of events = 796)

HR = 0.840 (0.76-0.92)
p < 0.0003


### Outcomes

- **MI**
  - RRR: -20.0% (p=0.003)
  - RRR: -22.0% (p=0.005)
  - RRR: 0% (p=1.0)
  
- **Stroke**
  - RRR: -24.0% (p=0.09)
  - RRR: -6% (p=0.84)
  
- **CV Death**
  - RRR: -26.0% (p=0.0002)
  - RRR: -14% (p=0.107)
  
- **Total Mortality**
  - RRR: -16.0% (p=0.0053)
  - RRR: -11% (p=0.13)
  - RRR: -11% (p=0.13)
  - RRR: -4% (p=0.43)

### Summary

- **n=929**  
  - MI: RRR: 0% (p=1.0)
  - Stroke: RRR: -6% (p=0.84)
  
- **n=12,218**  
  - MI: RRR: -22.0% (p=0.001)
  - Stroke: RRR: -24.0% (p=0.09)
  - CV Death: RRR: -14% (p=0.107)
  
- **n=8290**  
  - MI: RRR: -20.0% (p=0.003)
  - Stroke: RRR: -32.0% (p=0.0003)
  - CV Death: RRR: -26.0% (p=0.0002)
  - Total Mortality: RRR: -16.0% (p=0.0053)
  
**p-values**:
- MI: 0.001
- Stroke: 0.84
- CV Death: 0.107
- Total Mortality: 0.43

**Abbreviations**:
- MI: Myocardial Infarction
- CV: Cardiovascular
Overall Survival

Number at Risk

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<tr>
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<th>Years</th>
<th>Number at Risk</th>
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<tr>
<td>Medical Therapy</td>
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<td>1138</td>
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<tr>
<td></td>
<td>1</td>
<td>1073</td>
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<td>488</td>
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<td>6</td>
<td>312</td>
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<td></td>
<td>7</td>
<td>44</td>
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</table>

PCI + OMT

OMT

Hazard ratio: 0.87
95% CI (0.65-1.16)
P = 0.38
AVERT: Time to First Ischemic Event

Cumulative incidence (%)

Time since randomization (months)

Angioplasty/UC (n=177)

Atorvastatin (n=164)

p=0.027

Pitt et al NEJM 1999;341:70-76
Survival Free of Death from Any Cause and Myocardial Infarction

Number at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>Years</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<td>1138</td>
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<td>638</td>
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<tr>
<td>PCI</td>
<td></td>
<td>1149</td>
<td>1013</td>
<td>952</td>
<td>833</td>
<td>637</td>
<td>417</td>
<td>200</td>
<td>3</td>
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</table>

Hazard ratio: 1.05  
95% CI (0.87-1.27)  
P = 0.62
<table>
<thead>
<tr>
<th>Treatment Targets</th>
<th>Baseline</th>
<th>60 Months</th>
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<tbody>
<tr>
<td></td>
<td>PCI +OMT</td>
<td>OMT</td>
</tr>
<tr>
<td>SBP</td>
<td>131 ± 0.77</td>
<td>130 ± 0.66</td>
</tr>
<tr>
<td>DBP</td>
<td>74 ± 0.33</td>
<td>74 ± 0.33</td>
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<tr>
<td>Total Cholesterol mg/dL</td>
<td>172 ± 1.37</td>
<td>177 ± 1.41</td>
</tr>
<tr>
<td>LDL mg/dL</td>
<td>100 ± 1.17</td>
<td>102 ± 1.22</td>
</tr>
<tr>
<td>HDL mg/dL</td>
<td>39 ± 0.39</td>
<td>39 ± 0.37</td>
</tr>
<tr>
<td>TG mg/dL</td>
<td>143 ± 2.96</td>
<td>149 ± 3.03</td>
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<tr>
<td>BMI Kg/M²</td>
<td>28.7 ± 0.18</td>
<td>28.9 ± 0.17</td>
</tr>
<tr>
<td>Moderate Activity (5x/week)</td>
<td>25%</td>
<td>25%</td>
</tr>
</tbody>
</table>

LDL of 1.85 mmol/L
Blinded Coronary CT Angiogram\(^1\)

Core lab anatomy eligible?\(^2\)

no \(\rightarrow\) Screen failure

yes \(\rightarrow\) RANDOMIZE

INVASIVE Strategy
OMT\(^3\) + Cath +
Optimal Revascularization

CONSERVATIVE Strategy
OMT\(^3\) alone
Cath reserved for OMT failure

Average 4 Years of Follow-up
Primary Endpoint: Composite of CV Death and MI\(^4\)

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\(^1\) Coronary CT Angiogram will be performed in all patients with eGFR $\geq 60$ mL/min

\(^2\) Exclude patients with Left Main disease or no obstructive disease

\(^3\) OMT = Optimal medical therapy

\(^4\) Sample size estimation: Invasive vs. Conservative (17.2\% vs. 19.8\% at 5.5 years; 15\% RRR; two-sided alpha=0.05; 92\% power)
Performance Matters!
Relationship between Process and Outcome

In-hospital Mortality

% of Patients

n=45,987 with NSTEACS, 403 U.S. hospitals, Apr 2000-03

p<0.0001

<65%  65-75%  75-80%  >80%
5.89  4.98  4.55  3.57

Hospital Composite Adherence* Quartiles

* Use of 9 ACC/AHA Class I care indicators among eligible pts without contraindications (adjusted for pt + hospital features)

Adapted from Peterson et al J Am Coll Cardiol 2004;43(suppl.):406A
Performance Matters!
Changes in Hospital Non-ST ACS Guideline
Adherence and Patient Outcomes

Relative Change in Hospital Mortality Rates (%)

Every 10% ↑ in guidelines adherence → 11% ↓ in mortality

n=21,588 from 315 U.S. hospitals participating for ≥3 quarters

Peterson et al Circulation 2004;110:III-785
Use of a Treatment Optimization Algorithm Involving Statin-Ezetimibe Combination Aids in Achievement of Guideline-Based Low-Density Lipoprotein Targets in Patients With Dyslipidemia at High Vascular Risk

Guideline-Based Undertaking to Improve Dyslipidemia Management in Canada (GUIDANC)

Pamela M. Katz, Aurora A. Mendelsohn, Shaun G. Goodman, Anatoly Langer, Hwee Teoh, Lawrence A. Leiter,

Inclusion Criteria:
1. High Risk
2. On Statin already
3. LDL not at target

Algorithm:
1. Optimize Statin
2. Add ezetimibe
Achieving the Target LDL

Ezetimibe was started or continued on top of statin

<table>
<thead>
<tr>
<th>Visit</th>
<th>2006 Target: LDL-C &lt; 2.0 mmol/L</th>
<th>2009 Target: LDL-C &lt; 2.0 mmol/L or 50% or greater LDL-C reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visit 1</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Visit 2</td>
<td>6.8</td>
<td>36.3</td>
</tr>
<tr>
<td>Visit 3</td>
<td>43.3</td>
<td>45.5</td>
</tr>
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</table>

26.7% 33.7% 37.7%
Summary: OMT works and should be the standard of care

- Target achievement driven not prescription
  - Ensures optimal use rather than lowest possible dose

- Comprehensive in scope
  - Address all aspects at once
  - Use the right (evidence-based) therapy

- Incentivise the patient: longer and better life
  - Quote the risk directly
  - Quote the benefit numerically
  - Document recommendation in the chart

- Optimize and up titrate decisively
  - All the benefit may be in the move from starting to optimal dose