Over-the-Counter Statins: The Debate Continues…

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Objectives

1. Provide an overview of cardiovascular disease including risk factors, morbidity and mortality, prevention, and treatment
2. Discuss the 2011 heart disease and stroke statistics and forecast the future of cardiovascular disease in the United States
3. Evaluate the arguments for and against FDA approval of OTC statins in the United States
4. Assess current opinions of healthcare providers and formulate recommendations regarding OTC statin availability
I. Today’s Relevance

A. Pharmaceutical company Pfizer may seek OTC status for its cholesterol-lowering agent Lipitor® upon patent expiration in November 2011¹
   i. OTC version would allow Pfizer to retain a portion of the current $11 billion in annual revenue Lipitor® currently generates²
   ii. Convincing the Food and Drug Administration (FDA) will be difficult
       3. Prescription to OTC switches have been rare in recent years
   iii. Official statement from Pfizer: “We can confirm that we have strategic plans in place for Lipitor’s loss of exclusivity and will comment no further at this time.”¹

B. Heart Disease and Stroke Statistics – 2011 Update³
   i. Death rates from cardiovascular disease [CVD] have declined, yet the burden of disease remains high
      1. More than 2200 Americans die of CVD each day (1 death every 39 seconds)
      2. 785,000 Americans will have a new coronary attack and 795,000 Americans will have a new or recurrent stroke each year
   ii. Prevalence and control of traditional risk factors remains an issue
      1. 33.5% of US adults ≥20 years have hypertension (76,400,000 Americans)
      2. 23.1% of men and 18.3% of women age ≥18 years are cigarette smokers
      3. 15% of US adults ≥20 years have total cholesterol ≥240 mg/dL (33,600,000 Americans)
      4. 8% of US adult population have diagnosed type 2 diabetes mellitus [T2DM] (18,300,000); 7,100,000 Americans have undiagnosed T2DM; 36.8% of the US adult population have pre-diabetes (disproportionate in minorities)
   iii. The obesity epidemic continues to grow
      1. 67.3% of adults age ≥20 years is overweight or obese (149,300,000 adults)
      2. 31.9% of children age 2-19 years is overweight or obese (23,500,000 children)
   iv. The cost of CVD continues to grow
      1. The total direct and indirect cost of CVD in the US is $287 billion
      2. CVD costs more than any other diagnostic group
         a. For example, cancer and benign neoplasm cost $228 billion

C. Forecasting the Future of Cardiovascular Disease in the United States⁴
   i. By 2030, 40.5% of the US population is projected to have some form of CVD
   ii. Between 2010-2030, total direct medical costs of CVD are projected to triple (from $273 billion to $818 billion)
   iii. Total indirect costs of CVD are estimated to increase from $172 billion to $276 billion in 2030 (61% increase)

II. Cardiovascular Disease Overview

A. Diagnostic categories
   i. Coronary heart disease (CHD)
      1. Myocardial infarction (MI)
      2. Angina pectoris
      3. Heart failure
      4. Coronary death
   ii. Cerebrovascular disease
      1. Stroke
      2. Transient ischemic attack (TIA)
iii. Peripheral artery disease (PAD)
iv. Aortic atherosclerosis and thoracic or abdominal aortic aneurysm

B. Risk Factors
i. Atherosclerosis is responsible for the majority of cases of CHD
   1. Fatty streaks → lesions → plaques → thrombotic occlusions → coronary events

![Atherosclerosis Image](http://www.nlm.nih.gov/medlineplus/ency/imagepages/18050.htm)

Figure 1: Atherosclerosis - Fatty material is deposited in the vessel wall, resulting in narrowing and eventual impairment of blood flow to the heart muscle

ii. Approximately 50% of all patients with a CHD event have no established risk factors except for age and gender

iii. Modifiable Risk Factors
   1. Modifiable risk factors may account for 90% of the population-attributable risk of a first MI

<table>
<thead>
<tr>
<th>Table 1: Modifiable Risk Factors</th>
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<tbody>
<tr>
<td>Cigarette smoking</td>
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<tr>
<td>Abdominal obesity</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Renal disease</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Elevated LDL</td>
</tr>
<tr>
<td>Alcohol consumption</td>
</tr>
<tr>
<td>Stress</td>
</tr>
<tr>
<td>Physical Inactivity</td>
</tr>
<tr>
<td>Reduced HDL</td>
</tr>
</tbody>
</table>

2. Cigarette smoking
   a. Incidence of MI is increased 6-fold in women and 3-fold in men who smoke > 20 cigarettes/day compared to nonsmokers
   b. Risk of recurrent MI in a study of smokers fell by 50% within one year of smoking cessation and normalized to that of nonsmokers within two years

3. Abdominal obesity
   a. Associated with multiple CV risk factors – HTN, insulin resistance, glucose intolerance, hypertriglyceridemia, reduced-HDL, low levels of adiponectin
4. Hypertension
   a. Both systolic and diastolic blood pressure are risk factors for CVD
   b. Isolated systolic hypertension is a major risk factor for CHD and stroke

5. Physical Inactivity
   a. Moderate exercise has a protective effect against CHD and all-cause mortality
   b. In a retrospective study, men who engaged in moderate activity had a 23% lower risk of death compared to less active men

6. Renal Disease
   a. Mild to moderate renal dysfunction as well as end-stage renal disease is a risk factor for CHD
   b. National Kidney Foundation and American Heart Association recommended chronic kidney disease (CKD) to be a CHD risk equivalent

7. Diabetes mellitus
   a. National Cholesterol Education Program (NCEP) guidelines designated diabetes a CHD risk equivalent
   b. Copenhagen Heart Study suggest risk of incident of MI or stroke was increased 2-3 fold in type 2 diabetes and risk of death was increased 2-fold independent of other CHD risk factors
   c. Controversy exists regarding diabetes as a CHD risk equivalent – newly diagnosed T2DM patients may have low vascular risk and evidence may support an association with statins and new-onset diabetes

8. Elevated LDL
   a. Evidence of pathogenicity reported by randomized trials which suggest that reduced LDL-cholesterol levels decrease coronary events and death
   b. Dyslipidemia is common in patients with premature CHD (75-85 % compared to 40-48% in patients without CHD)

iv. Non-modifiable Risk Factors
   
<table>
<thead>
<tr>
<th>Age:</th>
<th>Males &gt; 45 years</th>
<th>Females &gt; 55 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of CAD</td>
<td></td>
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</tr>
</tbody>
</table>

1. Family history
   a. In the Framingham Offspring Study, 11% of offspring of the original Framingham cohort had a CV event at eight years of follow-up; subjects with > 1 parent with premature CVD had a significantly greater risk for cardiovascular events

III. Cardiovascular Disease Prevention
   
   A. Primary Prevention
      i. CVD remains the leading cause of death in the US and most developed countries
      1. Notable decline in mortality rates from CVD around the world
      ii. Aspirin is recommended for primary prevention by the United States Preventive Services Task Force (USPSTF) and by the American Heart Association (AHA) in patients at moderate to high risk of CHD
      iii. Modification of risk factors can dramatically reduce risk of CHD and stroke with the benefits being additive
1. Healthy diet, smoking cessation, treatment of hypertension, dyslipidemia, and T2DM, increase in physical activity, weight loss, and limited alcohol intake

iv. Risk Assessment

1. Framingham Risk Score (see Appendix 1,2)\(^{20}\)
   a. May overestimate or underestimate the risk of initial CHD events in populations such as Japanese American and Hispanic men, in Native American women, in European and Asian populations, in African American men and women, or in patients ≥85 years
   b. Does not include all potential consequences of atherosclerosis (stroke, TIA, HF)

2. SCORE (see Appendix 3)\(^{21}\)
   a. 2007 European Society of Cardiology guidelines on CVD prevention
   b. Estimates ten-year risk of any first fatal atherosclerotic event (not just CHD-related deaths) and estimates cardiovascular disease mortality

3. QRISK and QRISK2 (see Appendix 4)\(^{22}\)
   a. Predicts CV risk in patients from different ethnic groups living in England and Wales
   b. Includes risk predictors used in the modified Framingham model, as well as ethnicity, socioeconomic status, family history, and other medical variables (T2DM, CKD, atrial fibrillation, and rheumatoid arthritis)

4. Reynolds Risk Score (see Appendix 5)\(^{23}\)
   a. Outcome of stroke is included
   b. Includes all variables in the Framingham risk score as well as level of high-sensitivity C-reactive protein and parental history of MI <60 years of age

B. Secondary Prevention

i. Patients with established CHD have a high risk of subsequent CV events, including MI, stroke, and death from CVD\(^{20}\)

ii. Risk of future events is decreased by treatment of modifiable risk factors

1. Smoking Cessation
2. Blood Pressure Control
3. Physical Activity and Weight Management (goal 10% reduction in body weight)
4. Lipid Management

iii. Adjunctive drug therapies of proven benefit include aspirin, statins, and, in patients with MI or heart failure, beta blockers and ACE inhibitors

IV. Elevated Cholesterol Treatment

A. NCEP ATP-III Guidelines\(^{30}\)

i. Classification of LDL, Total, and HDL Cholesterol (mg/dL)

<table>
<thead>
<tr>
<th>LDL Cholesterol</th>
<th>Optimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td></td>
</tr>
<tr>
<td>100-129</td>
<td>Near optimal/above optimal</td>
</tr>
<tr>
<td>130-159</td>
<td>Borderline high</td>
</tr>
<tr>
<td>160-189</td>
<td>High</td>
</tr>
<tr>
<td>≥190</td>
<td>Very high</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Cholesterol</th>
<th>Desirable</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;200</td>
<td>Borderline high</td>
</tr>
<tr>
<td>200-239</td>
<td>High</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HDL Cholesterol</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>High</td>
</tr>
</tbody>
</table>
ii. Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals

- Cigarette smoking
- Hypertension (BP ≥140/90 mmHg or on antihypertensive medication)
- Low HDL cholesterol (<40 mg/dL)*
- Family history of premature CHD (CHD in male first degree relative <55 years; CHD in female first degree relative <65 years)
- Age (men ≥45 years; women ≥55 years)*

* In ATP III, diabetes is regarded as a CHD risk equivalent.
† HDL cholesterol ≥60 mg/dL counts as a “negative” risk factor; its presence removes one risk factor from the total count.

iii. Three Categories of Risk that Modify LDL Cholesterol Goals

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>LDL Goal</th>
<th>LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)</th>
<th>LDL Level at Which to Consider Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD or CHD Risk Equivalents (10-year risk &gt;20%)</td>
<td>&lt;100 mg/dL</td>
<td>≥100 mg/dL</td>
<td>≥130 mg/dL (100-129 mg/dL: drug optional)*</td>
</tr>
<tr>
<td>2+ Risk Factors (10-year risk ≤20%)</td>
<td>&lt;130 mg/dL</td>
<td>≥130 mg/dL</td>
<td>10-year risk 10-20%: ≥130 mg/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10-year risk &lt;10%: ≥160 mg/dL</td>
</tr>
<tr>
<td>0-1 Risk Factor†</td>
<td>&lt;160 mg/dL</td>
<td>≥160 mg/dL</td>
<td>≥190 mg/dL (160-189 mg/dL: LDL-lowering drug optional)</td>
</tr>
</tbody>
</table>

* Some authorities recommend use of LDL-lowering drugs in this category if an LDL cholesterol <100 mg/dL cannot be achieved by therapeutic lifestyle changes. Others prefer use of drugs that primarily modify triglycerides and HDL, e.g., niacin or fibrate. Clinical judgment also may call for deferring drug therapy in this subcategory.
† Almost all people with 0-1 risk factor have a 10-year risk <10%, thus 10-year risk assessment in people with 0-1 risk factor is not necessary.
### B. Treatment Options

<table>
<thead>
<tr>
<th>Drug Class, Agents and Daily Doses</th>
<th>Lipid/Lipoprotein Effects</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Clinical Trial Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMG CoA reductase inhibitors (statins)</td>
<td>LDL: ↓18-55%</td>
<td>Myopathy</td>
<td>Absolute: • Active or chronic liver disease</td>
<td>Reduced major coronary events, CHD deaths, need for coronary procedures, stroke, and total mortality</td>
</tr>
<tr>
<td></td>
<td>HDL: ↑5-15%</td>
<td>Increased liver enzymes</td>
<td>Relative: • Concomitant use of certain drugs¹</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TG: ↓7-30%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bile acid Sequestrants</strong>¹</td>
<td>LDL: ↓15-30%</td>
<td>Gastrointestinal distress</td>
<td>Absolute: • Dysbeta-lipoproteinemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HDL: ↑3-5%</td>
<td>Constipation</td>
<td>• TG &gt;400 mg/dl.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TG: No change or increase</td>
<td>Decreased absorption of other drugs</td>
<td>Relative: • TG &gt;200 mg/dl.</td>
<td></td>
</tr>
<tr>
<td><strong>Nicotinic acid</strong>²</td>
<td>LDL: ↓5-25%</td>
<td>Flushing</td>
<td>Absolute: • Chronic liver disease</td>
<td>Reduced major coronary events, and possibly total mortality</td>
</tr>
<tr>
<td></td>
<td>HDL: ↑15-35%</td>
<td>Hyperglycemia</td>
<td>• Severe gout</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TG: ↓20-50%</td>
<td>Hyperuricemia (or gout)</td>
<td>Relative: • Diabetes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Upper GI distress</td>
<td>• Hyperuricemia</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hepatotoxicity</td>
<td>• Peptic ulcer disease</td>
<td></td>
</tr>
<tr>
<td><strong>Fibric acids</strong>³</td>
<td>LDL (may be increased in patients with high TG): ↓5-20%</td>
<td>Dyspepsia</td>
<td>Absolute: • Severe renal disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HDL: ↑10-20%</td>
<td>Gallstones</td>
<td>• Severe hepatic disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TG: ↓20-50%</td>
<td>Myopathy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Concomitant use of certain drugs may lead to increased liver enzymes.
² Nicotinic acid may cause flushing, hyperglycemia, and hyperuricemia.
³ Fibric acids can increase liver enzymes and may cause dyspepsia and gallstones.
i. **HMG-CoA-reductase Inhibitors (statins)**

1. Competitively inhibits 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the enzyme that catalyzes the rate-limiting step in cholesterol biosynthesis.

![Diagram of cholesterol biosynthesis](http://www.nature.com/nrn/journal/v6/n4/images/nrn1652-f1.jpg)

Figure 5: Statins competitively inhibit the enzyme 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, which catalyzes the third and rate-limiting step of the cholesterol biosynthesis pathway.

2. **LDL-Lowering Comparison Chart (from package inserts)**

<table>
<thead>
<tr>
<th>% LDL Reduction</th>
<th>Atorvastatin</th>
<th>Lovastatin</th>
<th>Simvastatin</th>
<th>Pravastatin</th>
<th>Rosuvastatin</th>
<th>Pitavastatin</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30%</td>
<td>20 mg</td>
<td>10 mg</td>
<td>20 mg</td>
<td>20 mg</td>
<td>1 mg or 2 mg</td>
<td>4 mg</td>
</tr>
<tr>
<td>30-40%</td>
<td>10 mg</td>
<td>40 mg</td>
<td>20 mg</td>
<td>40 or 60 mg</td>
<td>5 mg</td>
<td>4 mg</td>
</tr>
<tr>
<td>40-45%</td>
<td>20 mg</td>
<td>80 mg</td>
<td>40 mg</td>
<td></td>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>46-50%</td>
<td>40 mg</td>
<td>80 mg</td>
<td>80 mg</td>
<td></td>
<td></td>
<td>20 mg</td>
</tr>
<tr>
<td>50-55%</td>
<td>80 mg</td>
<td>20 mg</td>
<td></td>
<td>20 mg</td>
<td></td>
<td>40 mg</td>
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<tr>
<td>56-60%</td>
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3. **The Statin’s Winding Road**

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1769</td>
<td>Cholesterol discovered in bile and gallstones</td>
</tr>
<tr>
<td>1823</td>
<td>“Cholesterine” discovered; later named cholesterol</td>
</tr>
<tr>
<td>1833</td>
<td>Cholesterol detected in blood for first time</td>
</tr>
<tr>
<td>1895</td>
<td>Cholesterol first linked to heart disease</td>
</tr>
<tr>
<td>1900</td>
<td>Families whose members have high cholesterol suffer from premature MIs</td>
</tr>
<tr>
<td>1901</td>
<td>Lowering cholesterol prevents heart attack</td>
</tr>
<tr>
<td>1950</td>
<td>LDL and HDL can be separated; LDL raises risk of CVD</td>
</tr>
<tr>
<td>1950s</td>
<td>Framingham Study finds that healthy people with high cholesterol have increased risk of MI</td>
</tr>
<tr>
<td>1962</td>
<td>Triparanol removed from market; falsified safety data</td>
</tr>
<tr>
<td>1964</td>
<td>Can describe how body makes cholesterol</td>
</tr>
<tr>
<td>1966</td>
<td>Oslo study: diet low in saturated fat lowers CVD risk</td>
</tr>
<tr>
<td>1978</td>
<td>Compactin taken by first person</td>
</tr>
<tr>
<td>1985</td>
<td>Role of LDL receptors discovered</td>
</tr>
<tr>
<td>1985</td>
<td>Mevacor approved; first statin in United States</td>
</tr>
<tr>
<td>1910</td>
<td>Cholesterol first linked to heart disease</td>
</tr>
<tr>
<td>1910</td>
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</tr>
<tr>
<td>1987</td>
<td>Mevacor approved; first statin in United States</td>
</tr>
<tr>
<td>1990</td>
<td>Lowering cholesterol prevents heart attack</td>
</tr>
<tr>
<td>1994</td>
<td>4S study: statins reduce MI mortality</td>
</tr>
<tr>
<td>1995</td>
<td>Cerivastatin recalled</td>
</tr>
<tr>
<td>2001</td>
<td>Cerivastatin recalled</td>
</tr>
<tr>
<td>2004</td>
<td>UK approves OTC simvastatin</td>
</tr>
<tr>
<td>2009</td>
<td>Pitavastatin approved; 7th statin on US market</td>
</tr>
<tr>
<td>2010</td>
<td>Annual MI mortality decreased 50% since 1980</td>
</tr>
</tbody>
</table>
ii. Bile Acid Sequestrants
   1. Bind to bile acids in the intestines, forming a complex that is excreted in the feces; increased bile acid excretion causes increased cholesterol catabolism to replace the bile acid

iii. Nicotinic Acid
   1. Decreases triglyceride levels by inhibiting release of fatty acids from adipose tissue as well as hepatic synthesis of fatty acids and triglycerides resulting in production of smaller, TG-poor VLDL particles, with subsequent inhibition of small, dense LDL production; may elevate HDL cholesterol levels by suppressing the hepatic removal of apo A-I

iv. Fibric Acid
   1. Activation of peroxisome proliferator activated receptor alpha [PPARα] increases the lipolysis and elimination of atherogenic triglyceride-rich particles from plasma by activating lipoprotein lipase and reducing production of apoprotein CIII; increase in the synthesis of apoproteins A-I and A-II, which leads to a reduction in LDL containing apoprotein B and an increase in HDL containing apoprotein A-I and A-II

V. OTC Statins – Bridging the Treatment Gap?

A. The Debate
   i. Arguments For
      1. Efficacy of statins has been established
      2. Will increase the prevalence of statin therapy in at-risk populations
      3. Will remove barriers to statin access
      4. Will decrease patient costs
      5. Rational as primary prevention in patients with limited comorbidities
      6. Will decrease cardiovascular morbidity and mortality

   ii. Arguments Against
      1. Limited assessment of patient by healthcare professional
      2. Safety in terms of comorbidities or drug-drug interactions
      3. Lack of monitoring for drug efficacy and adverse events
      4. Limited education on proper use
      5. Questionable ability of patient to self-select statin with limited information

B. The Standard
   i. OTC Simvastatin in Great Britain
      1. Practice Guidelines (see Appendix 6)
         a. In 2004, simvastatin 10 mg was reclassified from prescription-only to over-the-counter status in Great Britain
         b. OTC product license restricts sales to individuals at moderate ten-year risk of first coronary event
         c. Pharmacists must carry out a CV risk assessment but do not have to measure cholesterol or blood pressure

   2. Opinions of Healthcare Professionals
      a. British community pharmacists express confidence in making appropriate CV risk assessment
      b. Issues of concern related to evidence base to support OTC statin use, access to patient-specific clinical information, and the prohibitive cost
VI. Literature Review

<table>
<thead>
<tr>
<th>GENERAL STUDY OVERVIEW</th>
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<tbody>
<tr>
<td><strong>Title</strong></td>
</tr>
<tr>
<td><strong>Funding</strong></td>
</tr>
<tr>
<td><strong>Background</strong></td>
</tr>
<tr>
<td><strong>Trial design</strong></td>
</tr>
<tr>
<td><strong>Setting</strong></td>
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<tr>
<td><strong>Objectives</strong></td>
</tr>
<tr>
<td><strong>Enrollment</strong></td>
</tr>
</tbody>
</table>

**METHODS**

**Patient selection**
- All-comers; patients were recruited by mass media advertising to attract a population concerned about their cholesterol levels

**Interventions**
- MOTC-SMS was available to guide consumer behavior regarding cholesterol self-management
  - Shelf displays, product carton, package insert, Quick Start Guide, brochure, website, toll-free call center, cholesterol testing referral service, Consumer Assistance Program
  - Focused on primary prevention of CHD in individuals with multiple risk factors – “immediate risk population”
  - Label consistent with ATP III guidelines
- Nurse investigators assumed the role of trained pharmacists
  - Instructed not to volunteer information that could assist participant in the self-selection process
  - When requested could answer questions and perform eligibility assessment (script)
- MOTC label required that consumers know their HDL, LDL, and TG
  - Patients could purchase on-site cholesterol test if they inquired or leave study site to obtain previous levels or to talk to physician
  - Cholesterol panels were performed for all participants, but results were not released unless patients purchased a test
- Purchasers were able to purchase 1-4 cartons (45-day supply/carton)
  - Initial visit to study site and final visit (week 26) was scheduled
  - Purchasers could return to the store any time during the 26-week period to purchase more medication or for a cholesterol test
- Users’ behaviors were observed over the 26-week period

**Definitions**
- **Evaluator**: evaluated MOTC-SMS at study site
- **Purchaser**: purchased MOTC
- **User**: purchased and took ≥1 dose of MOTC
- **Non-purchaser**: did not purchase MOTC
- **Purchaser, non-user**: purchased MOTC but did not take
- **Self-selection**: initial use decision of the evaluator
- **De-selection**: ongoing use decisions over 26 weeks
- **Persistence**: percent users who completed ≥24 weeks treatment
- **Full adherence**: consuming 75%-120% of the intended tables (1 per day)
- **Compliance**: number of tablets taken divided by number of days of access to medications

**Statistical analyses**
- Descriptive statistics were utilized

**RESULTS**
- **Baseline characteristics**: Demographics similar between non-purchasers (n=2111) and users (n=1061)
- 41% of non-purchasers and 31% of users did not know LDL values at time of self-selection
- Average baseline LDL in users – 157 mg/dL
- 43% of non-purchasers and 57% of users had >2 CHD risk factors
- 80% of users had already tried diet/exercise
- 74% of users had discussed cholesterol with physician <2 years ago

Outcomes

- Will the right people use Mevacor OTC?
  - Most non-purchasers were ineligible for MOTC by label criteria
  - Most users were appropriate for therapy
  - Most users adhered or closely adhered to the label benefit criteria
  - 84% of evaluators appropriately decided to use or not to purchase MOTC
  - Most users who did not adhere to the label benefit criteria were eligible for statins (ATP III)
  - Most high CHD risk users interacted with their physician before self-selection
- Can consumers self-manage their cholesterol over time?
  - 71% of users obtained a follow-up cholesterol test (only includes those patients who were required to obtain)
- Will users of MOTC achieve beneficial lipid lowering in the OTC setting?
  - Persistence with therapy was 61% and compliance was 75% for 56% of all users
  - Among users who had fasting LDL at baseline and end of study, 25.2% reduction observed
  - Median LDL reduction of all users (fasting and non-fasting) was 20.6%
  - 62% of users with end-of-study LDL were at target LDL goal (<130)
- Will consumers involve their PCP in cholesterol self-management?
  - 29% of evaluators, 46% of non-purchasers, 42% of purchasers (before starting), and 57% of users interacted with their physician
- Will heart-healthy lifestyle behaviors improve?
  - 40% and 24% of users reported improvements in diet and exercise
- Can consumers manage potential safety risks?
  - 2% of users at the time of self-selection exhibited behavior associated with a potential safety concern (drug interactions, liver disease, use of antihyperlipidemic prescription)
  - 17% had drug-related AE; 12% discontinued MOTC because of AE; 0% rhabdomyolysis, myopathy, or acute liver disease

Authors’ Conclusions

The data from CUSTOM provide a compelling case for nonprescription availability of 20 mg of lovastatin. The MOTC-SMS has the potential to contribute to the prevention of CHD in the United States through consumers’ self-management of cholesterol and physician collaboration when more aggressive care is indicated.

Strengths and Limitations

Strengths:
- Study design replicated a natural retail setting
- Multiple geographic areas included increase external validity

Limitations:
- Funded by Merck Research Laboratories, the manufacturer of Mevacor
- Study not designed to accurately measure persistence or compliance
GENERAL STUDY OVERVIEW

Title
Consumer Behavior in the Setting of OTC Statin Availability: Lessons from the Consumer Use Study of OTC Mevacor

Citation

Background, Design, Setting, Objectives

METHODS

RESULTS

Baseline Characteristics

Outcomes

- Do consumers know their LDL cholesterol?
  - Self-reported and measured LDL values agreed 76% of the time
  - Patient with LDL >170 self-reported their level lower 8% of the time
- Do consumers make an appropriate use decision based on their risk stratification?
  - 34% of users had LDL >170; might be undertreated with lovastatin 20 mg
  - 22% of users had LDL<130; less risk reduction with lovastatin 20 mg
  - 24% of users had calculated 10-year risk >20% or had known CAD, DM, or stroke hx (42% of these patients reported using MOTC only after discussing it with their physician)
  - The diversion of high-risk patients from optimal care would result in an excess of 10.5 events per 100 patients over a 10 year period
  - Treatment of only 3 target consumers with MOTC who are not otherwise receiving statin therapy for each high-risk patient diverted from optimal care would result in net benefit
- Do consumers with potential clinically significant drug interactions decide not to use MOTC?
  - 80% of MOTC users who also took gemfibrozil checked with their doctors first
  - 66% of MOTC users who also took other lipid-lowering therapy checked with their doctors first
  - Concomitant drug use was self-reported and not independently verified which may underestimate actual usage
- Do consumers appropriately modify their self-management based on cholesterol assessments?
  - 70% of patients with data available obtained >1 follow-up cholesterol test during the study
  - 56% of patients were at target (LDL <130) and continued therapy
  - 5% of patients were above target and stopped therapy
  - 13% of patients were above target and continued therapy per physician
  - 25% of patients continued therapy despite high LDL
  - 26% of users continued to use MOTC without obtaining a follow-up cholesterol test
- Do consumers maintain/initiate relationships with healthcare providers after exposure to MOTC?
  - 62% of patients had discussed their cholesterol levels with their PCP within the previous year
  - 42% of patients who purchased MOTC discussed the drug with their PCP before using
  - 57% of users reported an interaction with their PCP (~ to those who discussed in last year)
  - 34% of users who had not discussed cholesterol in last 2 years interacted with their PCP
- Do consumers adhere to therapy with MOTC?
  - Persistence was estimated as 61%
  - Full adherence to treatment was estimated as 56%
  - Observational studies of RX statin therapy estimate persistence range of 40% over 12 months to 80% over 18 months in the structured VA setting
  - >85% of MOTC users reported using ≥1 aspect of the supporting materials (excluding package label) over the study period

AUTHORS’ CONCLUSIONS
The CUSTOM dataset provides estimates for the frequencies at which critical consumer behaviors occur that could potentially modify the risk-benefit ratio of OTC statin availability. The results show that large numbers of consumers not
currently on hypolipidemic therapy can use OTC statins safely and achieve desirable LDL cholesterol responses. The probable net public health effect of OTC statin availability appears to be reduction of CV events on a population basis, even accounting for the potential of higher-risk patients to divert from intensive therapy.

<table>
<thead>
<tr>
<th>Strengths and Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strengths:</strong></td>
</tr>
<tr>
<td>• Study design replicated a natural retail setting</td>
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<td>• Multiple geographic areas included increase external validity</td>
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<tr>
<td><strong>Limitations:</strong></td>
</tr>
<tr>
<td>• Funded by Merck Research Laboratories, the manufacturer of Mevacor</td>
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<tr>
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</tbody>
</table>
**GENERAL STUDY OVERVIEW**

<table>
<thead>
<tr>
<th>Title</th>
<th>Can Consumers Self-Select for Appropriate Use of an Over-the-Counter Statin? The Self Evaluation of Lovastatin to Enhance Cholesterol Treatment Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funding</td>
<td>None</td>
</tr>
<tr>
<td>Background</td>
<td>Large numbers of patients who meet the guideline recommendations for statins are not receiving the medication. OTC access to statins may improve treatment rates by expanding access to consumers and increasing awareness. Consumer behavior regarding the use of OTC statins was studied in the Consumer Use Study of OTC Mevacor (CUSTOM). Based on the results of CUSTOM, the proposed OTC label for lovastatin was modified. The effectiveness of these label changes was studied in the Self Evaluation of Lovastatin to Enhance Cholesterol Treatment (SELECT) study.</td>
</tr>
<tr>
<td>Trial design</td>
<td>Self-selection study</td>
</tr>
<tr>
<td>Setting</td>
<td>Simulation of a real-world OTC setting (Merck Research Laboratories, Pennsylvania)</td>
</tr>
<tr>
<td>Objectives</td>
<td>To assess consumers' ability to self-select for treatment with lovastatin in an unsupervised setting</td>
</tr>
<tr>
<td>Enrollment</td>
<td>5107 callers; 1528 visited study sites; 1326 made self-assessment decisions</td>
</tr>
</tbody>
</table>

**METHODS**

<table>
<thead>
<tr>
<th>Patient selection</th>
<th>Subjects recruited using mass-market advertising to attract a diverse population with concern about their cholesterol. Consumers:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Should know their cholesterol numbers</td>
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<tr>
<td></td>
<td>- Should call a toll-free number if interested</td>
</tr>
<tr>
<td></td>
<td>- Were given an appointment at a study site in their area</td>
</tr>
<tr>
<td></td>
<td>Callers were excluded if they did not read or understand English, were &lt;18 years old, had previously participated in a similar study, were a physician or pharmacist, or were referred to the study by another participant</td>
</tr>
<tr>
<td>Interventions</td>
<td>Self-selection process divided into 2 components:</td>
</tr>
<tr>
<td></td>
<td>- “Based on this label, is this product appropriate for you to use right now or not?”</td>
</tr>
<tr>
<td></td>
<td>- “Would you like to pay for this right now for your own use or put it back in the display?”</td>
</tr>
<tr>
<td></td>
<td>Label guided consumers through decision tree based on gender, age, LDL or total cholesterol, and presence of risk factors (hypertension, family history of heart disease, smoking, low HDL)</td>
</tr>
<tr>
<td></td>
<td>Instructed consumers they should not use if they had characteristics that put them at increased risk of adverse events from lovastatin based on health history or if clinical status suggested a need for more intensive cholesterol lowering</td>
</tr>
<tr>
<td></td>
<td>Subjects were given a proposed lovastatin carton with LDL cholesterol OR total cholesterol (TC) self-selection algorithm (alternating basis stratified by gender and site)</td>
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<tr>
<td></td>
<td>- Given opportunity to obtain cholesterol test</td>
</tr>
<tr>
<td></td>
<td>Demographic information, medical history, and cholesterol testing performed after decisions</td>
</tr>
<tr>
<td>Objectives</td>
<td>Based on self-assessment and purchase decisions, the primary objectives were to assess the ability of the new label to minimize self-selection by 3 consumer groups:</td>
</tr>
<tr>
<td></td>
<td>- Women &lt;55 years</td>
</tr>
<tr>
<td></td>
<td>- Women who are or may become pregnant</td>
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<tr>
<td></td>
<td>- Consumers with low absolute cardiovascular risk (Framingham 10-year risk score &lt;5%)</td>
</tr>
<tr>
<td></td>
<td>Secondary objective was to assess effectiveness of LDL cholesterol and total cholesterol algorithms in consumer decision making</td>
</tr>
<tr>
<td>Statistical analyses</td>
<td>Descriptive statistics</td>
</tr>
</tbody>
</table>

**RESULTS**

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>1326 subjects made Yes or No self-assessment decisions (662 LDL label, 664 TC label)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1457 subjects made purchase decisions (732 LDL label, 725 TC label)</td>
</tr>
<tr>
<td>Endpoints</td>
<td>Subjects assigned to LDL label</td>
</tr>
</tbody>
</table>
- 32% of subjects who evaluated LDL label said drug was appropriate for them
- Of those who indicated drug was appropriate, 82% met age criteria, 36% met LDL criteria, 82% had >1 additional risk factor
- 26% of subjects using LDL label strictly met all criteria for self-management per label algorithm
- 76% of subjects reported LDL corresponding to the correct band based on measured value (<130, 130-170, >170)

- Subjects assigned to TC label
  - 36% of subjects who evaluated TC label said drug was appropriate for them
  - Of those who indicated drug was appropriate, 85% met age criteria, 50% met TC criteria, 75% had >1 additional risk factor (women only), 55% met HDL criteria (women only)
  - 37% of subjects using TC label strictly met all criteria for self-management per label algorithm
  - 79% of subjects reported TC corresponding to the correct band based on measured value (<130, 130-170, >170)

- Women <55 years of age
  - 13% of women using LDL and 9% using TC label indicated drug was appropriate for them
  - Overall, 12% made a decision to purchase (compared to 24% in CUSTOM)
  - Pregnant women and women who may become pregnant
    - 4 women were pregnant; 1 decided lovastatin was appropriate; 0 decided to purchase
    - 22 women thought they might become pregnant; 2 decided lovastatin was appropriate for use; 0 decided to purchase
- Framingham 10-year risk <5%
  - 25% with 10-year risk <5%
  - 42% with 10-year risk 5-25%
  - 2.4% with risk >25%
  - 31% with known CHD, stroke, DM, currently using lipid-lowering therapy, missing data
- The 2 most common reasons to not purchase were a desire to speak with their PCP and recognition by the subject that they did not meet criteria for use
- 86 subjects who self-assessed Yes were on lipid-lowering medications
  - 58 indicated they would purchase the drug
  - 32/58 wanted to purchase the drug to use as a substitute for existing therapy

**AUTHORS’ CONCLUSIONS**

SELECT shows than an improved label facilitated appropriate self-selection based on a label algorithm designed to reflect NCEP primary prevention criteria while decreasing inappropriate use by women <55 years or who were pregnant or may become pregnant. Consumers might be more familiar with their total cholesterol than LDL cholesterol, and a TC-based algorithm may improve consumer utility. A major focus of CUSTOM was to decrease self-selection by women <55 years. The new label was effective in discouraging use (5.3% purchased in SELECT vs. 15% in CUSTOM). SELECT offered less guidance on self-selection than CUSTOM (only label and product carton); thus, SELECT may underestimate the positive impact of the label changes made. SELECT results combined with CUSTOM results provide evidence that consumers can safely and appropriately use OTC lovastatin in an unsupervised setting.

**Strengths and Limitations**

**Strengths:**
- Designed to reflect retail setting

**Limitations:**
- Study may not accurately represent a community pharmacy setting (appointment times given, etc)
- No hypothesis incorporated into protocol; all statistics were descriptive
- Resources to the consumer were limited to the label and product carton and results may not accurately reflect the effectiveness of consumer decision making
# GENERAL STUDY OVERVIEW

<table>
<thead>
<tr>
<th>Title</th>
<th>Impact of a Policy Allowing for Over-the-Counter Statins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funding</td>
<td>Grant from the Blue Cross and Blue Shield Foundation of South Carolina</td>
</tr>
</tbody>
</table>

## Background

Allowing statins to be sold without a prescription has been widely debated in Great Britain, Canada, and the United States. Some argue that OTC statins would increase the use of statins among those with moderate ten-year risk of coronary heart disease. In 2004, low dose simvastatin was reclassified in Great Britain as OTC status, and pharmacists carry out cardiovascular risk assessments without measuring cholesterol or blood pressure prior to sale. Pharmacists focus on risk factors like age, smoking, family history, weight, and race and are encouraged to assist patients in determining eligibility for statins. Little data exists regarding the impact of this policy and who is receiving treatment.

## Trial design

Analysis of the 2006 Health Survey for England (HSE) which focused on cardiovascular disease and risk factors

## Setting

Great Britain

## Objectives

To examine the impact of a recent policy in Great Britain allowing patients to purchase OTC simvastatin 10 mg on meeting the needs of individuals at moderate risk of coronary heart disease

## Enrollment

10007 patients; 1076 eligible for OTC statins

## METHODS

### Patient selection

- Study limited patients to adults aged 20 and older
- HSE is a yearly survey based on a nationally representative probability sampling design
- Patients who had not used statins within the last 7 days were excluded

### Variables

- Use of statins
  - “Are you taking or using any medicines, pills, syrups, ointments, puffers, or injections prescribed by a doctor?”
  - “Are you taking statins bought over the counter from a pharmacist, without a prescription from a doctor?”
  - “Have you taken/used any statins within the last seven days?”
- Eligibility criteria for OTC simvastatin (population categorized into 3 groups)
  - Individuals eligible for OTC simvastatin (males 55-70 years old, males 45-54 years with risk factor, females 55-70 years old with a risk factor)
  - Individuals who should be referred to a PCP because of higher risk of CHD or contraindication (hypersensitivity, history of muscle toxicity with statin or fibrate, individuals already taking RX cholesterol lowering drugs, concomitant administration of potent CYP3A4 inhibitors, active liver disease or unexplained persistent elevations of serum transaminases, pregnancy and breastfeeding, women of childbearing potential) to statins
  - Individuals who presumably do not warrant statin therapy

### Statistical analyses

Chi square analysis comparing differences between individuals meeting different criteria and OTC statin use; logistic regression examining relationship between age, gender, disadvantaged status, and OTC statin eligibility

## RESULTS

### Baseline characteristics

- Characteristics of those eligible for OTC statins
  - 75.6% 45-64 years; 24.4% >65 years
  - 65.4% male; 34.6% female
  - 92.9% white; 7.1% non-white
  - 49.8% disadvantaged (low education or low income or minority)

### Variables

- 44.1% of total adult population met criteria to be referred to a PCP for CHD risk
- 9.7% met eligibility criteria for OTC statins
  - 0.2% of patients eligible for OTC statins were actually taking them
  - 46.1% did not meet eligibility for prescribed or OTC statin therapy
  - 0.7% of the total adult population were taking OTC statins
  - Among those taking OTC statins, 79.9% met criteria for being referred to PCP, 18.1% did not
meet criteria for statins, and 2% met criteria for eligibility for OTC statins

- Characteristics of patients taking OTC statins
  - 15.7% 20-44 years; 35.5% 45-64 years; 48.8% >65 years
  - 50.9% male; 49.1% female
  - 85.4% white; 14.6% non-white
  - 72.3% disadvantaged
  - 28.2% told they have high cholesterol
  - 35.5% currently have high cholesterol
  - 71.5% using prescribed lipid lowering agents (overlapped with OTC statin use – 4.2% of patients taking OTC statins were also taking prescribed statins)

- Significant relationship between disadvantaged individuals and OTC statin use independent of age, gender, and eligibility

**AUTHORS’ CONCLUSIONS**

The aim of addressing the treatment gap among individuals at moderate risk by offering access to OTC statins has not been achieved two years after the implementation of the policy. Few people at risk are using OTC statins and the majority of individuals using OTC statins are either not in the target population or are concurrently using prescribed lipid lowering agents. The lack of OTC statin use may be because the eligible patient population is not getting the message from the healthcare sector that they are at risk for CVD.

**Strengths and Limitations**

**Strengths:**
- Data from nationally represented Health Survey for England; external validity
- Large sample size

**Limitations:**
- Data from 2006 and study published in 2010; may not accurately reflect impact
- Data from 2006 (2 years after implementation of policy); may not accurately reflect impact
- Information is self-reported and may be affected by recall bias or consumer confusion
GENERAL STUDY OVERVIEW

<table>
<thead>
<tr>
<th>Title</th>
<th>Socioeconomic and Ethnic Differences in Use of Lipid-lowering Drugs after Deregulation of Simvastatin in the UK: The Whitehall II Prospective Cohort Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Funding</td>
<td>Medical Research Council; British Heart Foundation; Health and Safety Execute; Department of Health; Agency for Healthcare Policy Research; John D and Catherine T MacArthur Foundation; National Heart, Lung, and Blood Institute and Nation Institute on Aging</td>
</tr>
<tr>
<td>Background</td>
<td>The stated rationale of OTC statins was an attempt to improve access to medicines, although some identified a financial motive. The shift in availability of OTC simvastatin may worsen health inequality, because those with more resources may be more likely to purchase OTC statins or because awareness of risk of CHD may influence purchasing.</td>
</tr>
<tr>
<td>Trial design</td>
<td>Prospective cohort study</td>
</tr>
<tr>
<td>Setting</td>
<td>Great Britain</td>
</tr>
<tr>
<td>Objectives</td>
<td>To examine the extent to which the use of lipid-lowering drugs, both prescribed and OTC, differed between socioeconomic and ethnic groups after deregulation, in adults with both moderate and high CHD risk</td>
</tr>
<tr>
<td>Enrollment</td>
<td>6967 participants at baseline; 6276 participants at follow up; 3631 participants analyzed</td>
</tr>
</tbody>
</table>

METHODS

<table>
<thead>
<tr>
<th>Variables</th>
<th>Socioeconomic position and ethnicity</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>- Assessed by British civil service grade of employment in 2002-2004 (classified as high, intermediate, or low positions)</td>
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<tr>
<td></td>
<td>- Ethnic group was observed at screening and classified as Caucasian, South Asian, Afro-Caribbean, Chinese, Other, or Uncertain (Chinese or other grouped together)</td>
</tr>
<tr>
<td></td>
<td>Use of lipid-lowering drugs and awareness of CV risk after deregulation of statin use</td>
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<tr>
<td></td>
<td>- At follow up, participants asked to list medications taken in the last 14 days, state if prescribed by doctor, and asked “Have you ever been told you have an increased risk of heart disease?”</td>
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<tr>
<td></td>
<td>- MMSE assessed cognitive ability</td>
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</tbody>
</table>

| Statistical analyses | Fisher exact test and analysis of variance to examine group differences in categorical and continuous variables |

RESULTS

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>1218 participants with moderate risk; 2911 participants with high risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- 96.6% and 84.2% respectively were available for follow up</td>
</tr>
<tr>
<td></td>
<td>Prior to deregulation of simvastatin</td>
</tr>
<tr>
<td></td>
<td>- Moderate risk: 95.8% white, 2.9% South Asian, 1% Afro-Caribbean, 0.3% other; 53.2% high employment grade, 40.9% intermediate, 6% low</td>
</tr>
<tr>
<td></td>
<td>- High risk: 88.7% white, 7.6% South Asian, 2.9% Afro-Caribbean, 0.9% other; 44.5% high employment grade, 44.3% intermediate, 11.3% low</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Use of prescribed lipid-lowering medications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- 20% with moderate risk and 44.1% with high risk reported using a prescribed lipid-lowering drug (p&lt;0.001)</td>
</tr>
<tr>
<td></td>
<td>- Ethnic differences in prescribed drug use: South Asian were more likely to report using a prescribed drug than Caucasian participants (p=0.001)</td>
</tr>
<tr>
<td></td>
<td>- Age positively associated with use (p&lt;0.01 for each additional year)</td>
</tr>
<tr>
<td></td>
<td>- Analysis of socioeconomic use revealed no difference</td>
</tr>
<tr>
<td></td>
<td>Use of OTC simvastatin</td>
</tr>
<tr>
<td></td>
<td>- 3.4% with moderate risk and 2.7% with high risk reported using any OTC drugs</td>
</tr>
<tr>
<td></td>
<td>- All reported OTC drugs were Omega-3 fatty acids; 0% OTC simvastatin use reported</td>
</tr>
<tr>
<td></td>
<td>Recall of CHD risk</td>
</tr>
</tbody>
</table>
| | - 21% with moderate risk and 44.1% with high risk remember being told they were at
increased risk of heart disease (p<0.001)
- Better recall associated with higher Framingham score (p<0.001)
- Among moderate risk participants, no association between ethnicity, employment grade and recall of CHD risk; age was inversely associated with recall (p<0.001 for each additional year)
- Among high risk participants, South Asian participants were less likely to recall than White participants (P=0.02); participants with intermediate and low employment were less likely to recall (p=0.001 and p<0.001) than those of high employment; no association with age

**AUTHORS’ CONCLUSIONS**

The stated rationale of deregulating simvastatin to widen availability seems to have had no impact on the problem of under-treatment. Early controversy around deregulation including fears of worsening health inequities seem to have been unfounded because the OTC product was not taken up. Those at highest risk of CHD have the poorest recall of their risk status. Sub-optimal prescribing remains an issue and that making drugs available for self-purchase is an ineffective response to the problem.

**Strengths and Limitations**

| Strengths: |
| Propective data collection |

| Limitations: |
| Loss to follow up |
| Many analyses were unable to reach statistical significance secondary to small sample size |
| Limited generalizability in some analyses |
| Self-reporting may lead to bias |

**VII. Conclusion**

**A. The Future**

i. FDA Review Process\(^2\)

1. FDA advisory committees make recommendations to the FDA concerning approval of drugs (both prescription only and over-the-counter)
2. From 1976 to 2002, the FDA approved 88 switches from prescription only to OTC status, most reviewed by Nonprescription Drugs Advisory Committee (NDAC)
3. Each committee consists of a standing panel of outside experts selected from a list of nominees by the FDA commissioner, a voting consumer representative, a nonvoting industry representative, and a variable number of invited voting consultants who are not standing members
4. Each NDAC meeting contains an open public hearing that lasts at least 1 hour
5. Shortly before the meeting, NDAC advisory committee members receive information from the FDA on the relevant clinical trials and a list of question to be addressed concerning drug safety and efficacy, whether the consumer can use the medication without guidance or direct consent of a physician, and whether the committee recommends a switch from prescription to OTC status
6. NDAC committee members are asked to only consider safety, efficacy, and the appropriateness of self-diagnosis and self-medication

**B. What Our Profession Asserts\(^3\)**

i. ASHP Statement on Over-the-Counter Availability of Statins (2005)

1. Existing models for OTC dispensing do not provide the safeguards required to ensure the safe and effective use of statins as part of a multimodal approach to preventing CHD
2. ASHP supports the goal of more widespread use of CHD-preventive therapies, including statin therapy, and encourages consideration of alternative nonprescription dispensing models for statins that would advance CHD prevention
3. To achieve the goal of safe and effective use, any nonprescription dispensing model for statins should:
   a. Identify candidates for appropriate therapeutic interventions on the basis of cholesterol levels, other risk factors for CHD events, and the patient’s history
   b. Allow patients and health care providers to monitor response to treatment, including adverse reactions
   c. Maximize the effectiveness of treatment by encouraging adherence to therapy and appropriate interactions with health care professionals.
4. ASHP believes that before a patient begins statin therapy, a cardiac risk assessment should be performed by a competent health care professional in order to:
   a. Determine the patient’s LDL-C value, which can be used as a baseline value if the patient is a candidate for treatment
   b. Assess the individual for other cardiovascular risk factors such as smoking, diabetes, hypertension, diet, weight, amount of exercise, and family history of CVD
   c. Develop the optimal treatment plan based on ATP III guidelines and assessment

C. OTC Statins – To Be or Not to Be
   i. Is the benefit worth the risk?
      1. Benefit-to-risk ratio associated with statin use is high in patient with high risk of CV event; however, in patients at lower risk, benefit-to-risk ratio is lower
         a. Statin-induced adverse events may outweigh benefits in patients at low risk of CV events
         b. Patients at high risk may purchase OTC statin when they should be treated by a healthcare professional
   2. OTC statin users may be inadvertently prescribed drugs that increase the risk of a drug-drug interaction
      c. Transplant patient taking cyclosporine
      d. Patient with infection prescribed erythromycin
      e. Patient being treated with gemfibrozil or prescription-only statin
   3. Elderly users of OTC statins may be at an increased risk for adverse effects
      f. Patients already taking multiple medications may add to the risk of adverse effects associated with unmonitored use of statins
   ii. Will we be able to achieve the recommended LDL goal?
      1. Unmonitored, low dose statin available OTC may be insufficient to achieve recommended LDL
   iii. Can we ensure compliance?
      1. The ability to purchase OTC statin will eliminate the ability to monitor for refill compliance; patients may be lost to follow up
      2. The National Council for Patient Information and Education has reported that 75% of patients don't take their medications as prescribed, 49% of patients forget to take their medication while 31% of patients don't fill their prescriptions; these numbers may increase with OTC medications
VIII. References


