# Burden of Disease: Medical and Economic Impact of Acute Coronary Syndromes

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***Abstract***

Despite advances in treatment, acute coronary syndromes (ACS), which consist mainly of ST-segment elevation myocardial infarction (STEMI) and unstable angina (UA)/non-STEMI (NSTEMI), present an enormous medical, social, and economic burden worldwide. According to public databases, 879 000 patients were discharged from US hospitals with a diagnosis of ACS in 2003. Globally, ACS in the form of myocardial infarction are responsible for almost half of all deaths related to cardiovascular disease. One third of STEMI patients die within 24 hours of onset, and about 15% of UA/NSTEMI patients will die or experience reinfarction within 30 days.

ACS also exact a high toll in terms of treatment-related and indirect economic costs. Direct medical costs of ACS are estimated at $75 billion, with a significant portion going toward drug therapy and associated costs. Data from clinical trials indicate that a management strategy including antithrombotic therapy can reduce ACS-related morbidity and mortality and related costs. More recently developed antithrombotic agents may have clinical and economic advantages over older therapies.

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Acute coronary syndromes (ACS) are ischemic cardiovascular pathologies ranging from unstable angina (UA) and non–ST-elevation myocardial infarction (NSTEMI) to classic transmural myocardial infarction (MI) with ST-segment elevation (STEMI). In contrast to STEMI, both UA and NSTEMI are often accompanied by ST-segment depression, and are closely related to one another in etiology, clinical course, and prognosis.[1,2] The term UA is used to describe a variety of symptom complexes that are more severe and unpredictable than stable angina but less so than classic MI. UA is commonly defined as angina pectoris with symptoms occurring at rest or with minimal exertion and lasting for at least 10 minutes, or with severe symptoms occurring either for the first time or becoming more frequent, severe, or prolonged than they had previously been. A diagnosis of NSTEMI is made when a patient with UA exhibits signs of myocardial necrosis, as evidenced by the appearance in serum of troponins or other biomarkers of cardiac injury but without ST-segment elevation on the electrocardiograph.[2-4] Despite recent advances in their treatment, both STEMI and NSTEMI, as well as UA, continue to present an enormous burden worldwide in terms of their medical, social, and economic cost.

## ACS: Scope of the Problem

ACS are a major source of mortality and morbidity both during and after hospitalization,[1,5] with up to 30% of discharged patients needing rehospitalization within the first 6 months.[6] According to the Centers for Disease Control and Prevention and the National Center for Healthcare Statistics, 879 000 patients were discharged in 2003 from hospitals in the United States with a diagnosis of ACS. Of these, an estimated 497 000 were men and 382 000 were women. When secondary discharge diagnoses are included, the number of hospital discharges was 1 555 000 hospitalizations for ACS, 946 000 for MI, and 650 000 for UA. There were 31 000 hospitalizations with both MI and UA.[7] There are variations in the standards of care among centers and among specialties.[8-10]

MI (STEMI and NSTEMI) occurs in approximately 865 000 persons annually in



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the United States, and about one sixth of these individuals die before being hospitalized.[2,7] It is estimated that only about 20% of these attacks are preceded by long-standing angina.[7] On a global scale, MI is probably responsible for 40% to 50% of all mortality related to cardiovascular disease.[11] Data from the Family Heart Study (FHS) of the National Heart, Lung, and Blood Institute show that 25% of men and 38% of women will die within 1 year of having an initial, recognized MI,[7] and mortality (including sudden death) among patients with UA ranges from 8% to 13% at 6 months.[12,13] According to the FHS, 18% of men and 35% of women experience a second MI within 6 years after having a recognized first attack. Within this same interval, heart failure will disable approximately 22% of men and 46% of women who have had an MI, and 8% of men and 11% of women will experience a stroke.[7]

Approximately one third of patients with STEMI (who represent an estimated 30% to 45% of ACS cases[7]) die within 24 hours of the onset of ischemia, and many of the survivors suffer significant morbidity afterward.[4] Like STEMI, UA and NSTEMI are life-threatening, major causes of emergency medical care and hospitalization.[1,2,12] Among patients with UA or NSTEMI, approximately 15% will die or have a reinfarction within 30 days of diagnosis,[3] and about 30% of patients with UA will have an MI within 3 months.[12] In 1996, UA and MI were together responsible for a reported 1 443 000 hospitalizations in the United States.[1,3] UA is the primary diagnosis in approximately 800 000 hospitalizations annually, and a similar number of episodes probably go unrecognized or are managed in outpatient settings.[14] Early data from the CRUSADE [Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA* Guidelines] Registry indicate an inhospital mortality rate of 4.5%, compared with less than 2% reported in other ACS trials.[15]

As with many other diseases, the prevalence of ACS increases with age. Of the more than 1.4 million persons hospitalized for ACS in 1996, almost 60% were 65 years of age or older.[1] In the Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) IIb study of coronary vascular occlusion, the median age for those with acute STEMI was 63 years, whereas that for patients with NSTEMI was 66 years.[16] Predictions for the year 2020 and beyond suggest that ischemic heart disease will be the leading cause of death and disability worldwide.[17] ACS are likely to remain a leading cause of hospitalization, both as a result of the aging population and also because of a growth in risk factors for coronary heart disease (CHD),[1-3] and will continue to present a major healthcare challenge in the foreseeable future.[1]

### ACS: Economic Burden

ACS exact a high toll in terms of direct, treatment-related and management costs, as well as indirect, social and economic costs.[18] Among direct US costs in 2006 for CHD, most of which consist of costs for ACS, physician and other professional costs are estimated at $11.1 billion, hospital costs at $41.8 billion, nursing-home costs at $10.9 billion, the cost of drugs and other medical durables at $9.8 billion, and home healthcare at $1.6 billion, for a total of $75.2 billion (**Table**).[7] Indirect US costs of CHD for 2006 (because of lost productivity) are estimated to be $142.5 billion (Table).

Clinical studies strongly suggest that a management strategy based on risk-stratification of the patient, thrombolytic and anticoagulant therapy, and when indicated, early percutaneous coronary intervention (PCI) and stenting, may reduce ACS-related morbidity and mortality and their attendant costs.[1,19] Among the means examined for achieving this goal has been the establishment of chest pain facilities. These facilities could be used to distinguish between patients in whom thoracic pain does or does not signify a serious risk for acute MI, to reduce unnecessary hospital admissions and occupancy of coronary care units,[20,21] and to increase the availability of catheter laboratory facilities and cardiologists for patients at greater risk.[21] Likewise, studies of the precision and cost efficacy of diagnosing ACS

*ACC/AHA, American College of Cardiology/American Heart Association.

**Table.** Estimated Costs of Cardiovascular Diseases (CVDs) and Stroke: United States, 2006

| Costs ($ Billion) | Heart Disease | CHD | Stroke | HTN | HF | Total CVDs |
|---|---|---|---|---|---|---|
| Direct costs | | | | | | |
| Hospital | 81.3 | 41.8 | 15.5 | 6.2 | 15.4 | 114.8 |
| Nursing home | 20.7 | 10.9 | 14.3 | 4.2 | 3.9 | 42.6 |
| Physicians/other professionals | 19.7 | 11.1 | 3.1 | 11.0 | 2.0 | 38.3 |
| Drugs/other | | | | | | |
| Medical durables | 21.2 | 9.8 | 1.3 | 24.4 | 3.1 | 50.1 |
| Home healthcare | 5.2 | 1.6 | 3.1 | 1.7 | 2.4 | 11.8 |
| Total expenditures* | 148.1 | 75.2 | 37.3 | 47.5 | 26.8 | 257.6 |
| Indirect costs | | | | | | |
| Lost productivity/morbidity | 21.9 | 9.6 | 6.4 | 7.7 | N/A | 35.6 |
| Lost productivity/mortality | 88.5 | 57.7 | 14.2 | 8.3 | 2.8 | 109.9 |
| Grand totals* | 258.5 | 142.5 | 57.9 | 63.5 | 29.6 | 403.1 |

*Totals do not add up because of rounding and overlap.
CHD indicates coronary heart disease; HTN, hypertensive disease; HF, heart failure; N/A, not available.
*Source:* Adapted from Reference 7.

have found, for example, that for a 55-year-old man with nonspecific (atypical) chest pain, treadmill-exercise echocardiography is the most cost-effective screening method (incremental cost-effectiveness ratio [ICER]: $41 900 per quality-adjusted life-year [QALY] saved), whereas routine coronary angiography is more cost-effective than treadmill-exercise echocardiography for a man of the same age with typical angina (ICER: $36 400 per QALY saved).[22]

The management strategy for ACS calls for treating evolving acute STEMI, and preventing the progression of UA and NSTEMI to acute STEMI and death, by hospitalization of the patient and the use of antiplatelet and anticoagulant therapy, either alone or in conjunction with early revascularization (either PCI or surgery).[1] The current practice guidelines of the ACC/AHA for patients with STEMI call for PCI no more than 12 hours (preferably within 90 minutes) after the onset of symptoms, or for pharmacologic thrombolytic therapy if PCI is unavailable; the guidelines recommend coronary artery bypass graft surgery for suitable patients who are not candidates for medical thrombolysis or PCI but who are still in the early, 6- to 12-hour stages of an evolving STEMI.[4] The 2002 update to the ACC/AHA guidelines for managing UA/NSTEMI calls for an early invasive strategy of angiography and revascularization for patients who have recurrent angina or ischemia at rest, elevated levels of cardiac troponins, new ST-segment depression, or any of several other risk factors.[3] The 2005 ACC/AHA updated guidelines for PCI also support use of early aggressive PCI in UA/NSTEMI.[23] A conservative strategy with planned revascularization may be offered in the absence of these findings.[3]

One component of the cost of ACS is pharmacotherapy, which includes antithrombotic agents such as unfractionated heparin (UFH) and low molecular weight heparins (LMWH).

Before the introduction of LMWH in the late 1980s, UFH was the mainstay of antithrombotic therapy,[24-26] and it is still widely used in the management of ACS.[1,4] The development of LMWH represents a major step in the quest for alternative antithrombotic agents to UFH.[1]

Produced by the degradation of heparin into shorter polysaccharide chains that contain the requisite site for binding to antithrombin to inactivate factor Xa and thrombin. LMWH do not bind as extensively to plasma and other proteins as UFH. Hence, they have greater bioavailability and a more predictable dose–response effect. This permits their use by subcutaneous injection

once or twice daily. It also obviates the need for the regular monitoring of clotting times that is needed with UFH.[13,27,28] Because of these favorable characteristics, using LMWH instead of UFH makes it possible to reduce hospital lengths of stay and their attendant costs for patients with ACS, by allowing antithrombotic treatment to continue on an outpatient basis.[28]

The predictable effects of LMWH, and the lack of need for coagulation monitoring with their use, have led to a significant increase in their utilization in the management of ACS.[29] But LMWH are considerably more expensive than UFH, and from a pharmacoeconomic perspective, this cost differential partially negates their advantages over UFH (such as decreased length of hospital stay). More recently, however, another class of antithrombotics, factor Xa inhibitors, have been studied in the setting of ACS. According to some large, randomized trials, the introduction of factor Xa inhibitors, such as fondaparinux, into the acute management of ACS could lead to clinical advantages as well as cost savings.[30,31]

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