Unhealthy ageing: functional and socioeconomic impact

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The long-term impacts of disease on functional status and on cost loom larger in the elderly than in any other age group. In older patients, the chronic sequelae of myocardial infarction and stroke often account for greater functional disability and resource utilization than does the initial acute presentation. In order to study this, quantitative measures from clinical and functional status assessments must be related to lifelong resource use. Rigorous measurement of such outcomes can render it possible to measure the impact on the health care system of specific cardiovascular and cerebrovascular consequences of ‘unhealthy ageing’. If performed in the context of a randomized clinical trial studying the effect of preventive measures, this approach can also lay the groundwork for assessment of the clinical and economic benefits of measures taken to reduce such morbidity. (Eur Heart J Supplements 2001; 3 (Suppl N): N3–N5) © 2001 The European Society of Cardiology

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Introduction

The generations that are alive today are participating in an unprecedented change in human demography. Throughout the industrialized world we are witnessing an increase in the proportion of society that is ‘elderly’, however that term is defined. This change is having profound effects on the health care delivery system, on family and social relationships, and on the economy. There is little in the human experience that we can turn to for guidance in navigating these uncharted waters, because these changes have never occurred before in this magnitude in all of human history. In fact, it has been estimated that, of all human beings who have ever lived past the age of 65 years, half are alive today.

The demographic tidal wave

The demographic experience in the U.S.A. is not dramatically different from that in the rest of the industrialized world. We can take age 65 years as a completely arbitrary benchmark to define ‘the elderly’. In 1900, approximately 4% of the population in the U.S.A. was older than 65 years; at present around 14% have reached this age, and we expect that by the year 2020, when the ‘baby boom’ generation enters this elderly cohort, approximately 20% of the population will be aged 65 years or older. In addition, this 20% of the population will be consuming far more than 20% of all health care resources. This is in part because the average age of the over-65 cohort is also increasing. Until very recently, those over 85 were the fastest growing segment of the U.S. population. Thus, not only is society ageing but also the average age of the aged is increasing.

Ageing versus disease

An important agenda for gerontology (the study of the ageing process in organisms and in societies) and for geriatrics (the care of elderly patients) is defining the distinction between disease and ageing. Despite existing stereotypes, the data make it clear that normal healthy ageing does not bring with it any degree of clinically important dementia, depression, fatigue, shortness of breath or incontinence. These are all caused by specific diseases, some of which are amenable to management and some are not yet so. However, even in the case of Alzheimer’s disease, for which we do not yet have any
really satisfying therapy, it is important to bear in mind that dementia in the elderly is still a discrete illness, and not a normal part of the ageing process. A very useful assumption is that if an elderly patient presents with a clinical problem then the first presumption should be that it is the result of a disease process, rather than the result of ‘just getting old’.

**Burden of illness**

With this ageing of the population, it is becoming increasingly important to be able to quantify the burden of illness in our ageing populations. This will be vital not only in planning for the necessary health services that will be required in the coming years, but also in order to measure the benefit that can be expected from interventions to prevent disability in the elderly.

In approaching this issue, it is important to understand that the analytical approach required for a conventional randomized clinical trial differs substantially from what is needed for population-level analyses. For example, consider a clinical trial of an antihypertensive medication, an anticoagulant or a lipid-lowering drug. In order to measure whether the drug reduces risk (e.g. for stroke or myocardial infarction), an end-point is defined, patients are randomized to treatment group or placebo, and the rate in which the clinical event occurs in each group is measured. This is the ‘gold standard’ for determining the efficacy of a given drug (or other preventive intervention), and for that purpose it is ideal.

In the lives of people (as opposed to experimental subjects), however, the burden of illness caused by stroke or myocardial infarction does not end once the ‘end-point’ is reached, even though from the trialist’s point of view that subject need no longer contribute further data to the trial. In the real world of patients, families and doctors, the burden of that myocardial infarction or stroke is likely to continue throughout the remaining lifespan of the person, bringing with it months and years of substantial disability. Furthermore, the event may be followed by another similar event, and another; alternatively, to think of it in a positive way, a successful preventive strategy may be followed by many years of disease-free existence long after the trial period has ended. These too are events (or non-events) that are generally not captured in the typical limited-term clinical trial.

Cognitive impairment, a particularly onerous burden in the elderly, reflects another paradox in the measurement of disease burden in the elderly. There may not be any ‘acute end-point’ event that is marked by hospitalization. Alternatively, hospitalization in the case of stroke may be extremely brief, and in no way indicative of the degree of disability that the stroke may cause for years to come. As a result, the analytic techniques that are appropriate for the assessment of efficacy in a clinical trial may be quite different from those that are needed to measure the impact of a given intervention on an ongoing basis, and in a real-world population viewed over time.

A related issue in geriatrics concerns the distinction between diagnosis and functional status. In order to conduct a clinically appropriate and policy-relevant assessment of the state of health of an older patient, it is not enough merely to identify a given diagnosis. Far more important is the impact that diagnosis has on the patient’s ability to get through the day and live their life. For example, one could describe a 78-year-old man who has coronary heart disease, cognitive impairment and benign prostatic hypertrophy, and has suffered a right-sided stroke. Each of these may be accurate diagnoses. Without further information concerning their impact on functional status, however, it would be impossible to know whether he is a functional but mildly impaired individual living independently in his own apartment, or (as a result of these very same diagnoses) he is a bed-ridden cripple requiring total care in a nursing home.

**The PROSPER trial**

These issues may be put into clearer perspective in relation to atherosclerosis if we consider how they are being applied in the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) trial, which is described in greater detail elsewhere in this supplement. This is a randomized, placebo-controlled trial of over 5000 elderly participants in Scotland, Ireland and The Netherlands, who are receiving either pravastatin or placebo in the first large-scale clinical trial devoted exclusively to measuring the impact of lipid-lowering medication in the elderly. Working with colleagues from the PROSPER team in each of the three study countries, our group at Harvard Medical School is coordinating the economic analysis of the trial, findings from which will become available in the coming year.

From the beginning, we felt that it was important to conduct this analysis in keeping with the geriatric insights described above. The primary analyses that will be performed in the trial will be of the conventional ‘gold standard’ type, measuring whether there are differences in the rates of specific clinical end-points (e.g. myocardial infarction, stroke) in patients randomized to the pravastatin group compared with those randomized to placebo. The work that my PROSPER colleagues and I are doing on the economic analysis begins where this standard analysis ends. We will be interested in looking at second and third events that may befall patients, and we will also be concerned with the functional status decrement that results from these specific clinical events. Furthermore, because the trial is only 3 years in duration, and patients take lipid-lowering medications throughout their lives, we will need to model the differences that would be seen in patients who continued to take pravastatin for the rest of their life compared with identical patients who never took pravastatin.

The analytic approach required here is rather complicated, and is described in a separate report. For the present purposes, however, it is sufficient to point out that such a disability-orientated, life-duration analysis is necessary in order to depict accurately the burden of illness (as well as health care costs) that such a cohort of patients...
would experience, as well as the degree of benefit that could be achieved (if this is what the trial finds) by eliminating a portion of that burden. Our analysis will attempt to take into account the lifelong consequences of the functional incapacity that result from stroke and myocardial infarction, as well as other outcomes. To do this, we will measure the reduction in risk, events, disability and health care utilization that are associated with the study treatment, based on the findings from the trial itself. We will then project these over time in order to measure the impact of such changes based on lifelong use of the drug, rather than the more arbitrary 3-year duration of therapy required by the randomized trial context.

Analyses such as this will become increasingly important in the coming years as health care systems throughout the world struggle with limited resources that surely will not grow as fast as the demands put on those systems by an ageing population. We live in a world in which health care demand is increasingly outstripping the resources available to meet that demand. More and more, it will be necessary to evaluate comprehensively the benefits of a given treatment (or diagnostic approach, or lifestyle change) in order to put it into context with other options that compete for the same constrained pool of resources.

**Conclusion**

Measuring the lifelong burden of disease, rather than counting the number of clinical events, is an approach that will come to define progressively more of our view of health care in the coming years. In an ageing society, these same issues will come up again and again in planning for the management of osteoporosis, hypertension, depression, incontinence, dementia, Parkinson’s disease and dozens of other conditions that are common in the elderly. Many of the methodological tools that are available to us are still evolving. We are embarking on a difficult and demanding agenda, but it is one that we must pursue in order to understand the nature and scope of the illness burden faced by our ageing populations, and the implications of that burden for preventive therapies.

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