Alzheimer’s disease (AD) is the most common cause of dementia, with an estimated prevalence of more than 106 million worldwide by 2050.\(^1\) It is a neurodegenerative disease characterised by the accumulation of senile plaques (deposits of the β-amyloid peptides) and neurofibrillary tangles (abnormal hyperphosphorylated insoluble forms of the tau protein). Patients with AD often experience problems of memory loss, confusion, impaired judgement, disorganised thinking, loss of ability to express themselves and disorientation with regard to time, space and location. AD progression leads to a significant deterioration in cognitive function, resulting in patients being increasingly bedridden and dependent on care-givers and, eventually, professional long-term care (LTC) such as nursing home care. AD has a substantial impact not only on the quality of life of ageing people, but also on the lives of family members and care-givers. The burden of AD may indicate dementia and to look for the signs requiring referral to a specialist for assessment. In fact, improving the diagnostic process in primary care represents a key step in increasing the number of cases detected in the population.

According to the French Personnes Agees Quid (PAQUID) cohort study, the Mini-Mental State Examination (MMSE) score at the time of diagnosis of dementia for the majority of cases is 16–20.\(^2\) so the diagnosis is established at the moderate stage of the disease in the majority of cases. In Europe, the average time required to establish the diagnosis of dementia (time between the onset of symptoms of the disease and diagnosis) is estimated at 20 months, which underlines the current level of late diagnosis.\(^3\) In 112 cases of dementia detected by general practitioners (GPs), the documentation rate was 33% for the mild stage of dementia, whereas it was 46 and 73%, respectively, for the moderate and severe stages.\(^4\) Furthermore, in many cases the initial symptoms do not alert the patient or relatives, as there is frequent confusion between ageing and dementia; also, when patients see a doctor, dementia is often not identified by the GP, which may be due to problems such as difficulties in distinguishing between a degenerative condition and cognitive recall with sensory problems or general conditions, or because of poor-quality information for practitioners relating to specifics about AD and the treatment to prescribe, etc. It is therefore important to provide GPs with information and practical tools that will help them recognise the symptoms that may indicate dementia and to look for the signs requiring referral to a specialist for assessment. For some physicians and other health professionals, the clinical diagnosis of AD presents a dilemma. Some physicians may feel that the stress related to a confirmed diagnosis may have a negative effect on the patient, especially as there are currently no curative treatments available. However, a lack of diagnosis can create a dangerous situation, as without any diagnosis most of these patients are likely to face several problems related to the symptoms of AD, such as poor...
Plan for Alzheimer’s Disease (PLASA) study.7 The oldest AD sufferers need early assistance such as defined in the Specific Care and Assistance Plan for Alzheimer’s Disease (PLASA) study. The oldest AD sufferers are expected to be prone to the greatest problems and should be given all the help needed as soon as possible.

**Diagnostic Criteria for Alzheimer’s Disease**

Diagnosis of AD is based on the prevailing criteria set out by either the National Institute of Neurological Disorders and Stroke–Alzheimer Disease and Related Disorders (NINDS-ADRDA) working group,8 or the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV-TR).9 The diagnostic process consists of two steps: initial identification of a dementia component followed by the application of criteria based on the clinical features of the AD phenotype. In recent years, understanding of the biological basis of AD has greatly improved and distinctive biomarkers of the disease have been identified. These biomarkers include structural brain changes visible on magnetic resonance imaging (MRI), molecular neuroimaging changes seen with positron emission tomography (PET), and changes in cerebrospinal fluid biomarkers.10 This progress in the elucidation of the development of AD and identification of biomarkers of disease has led to the proposal of revised diagnostic criteria for AD.11 These criteria aim to include both the earliest stages of disease, i.e. before confirmed dementia, and the complete range of disease stages. The core diagnostic criteria focus on the presence of early and significant episodic memory impairment. This should be complemented by the presence of at least one abnormal biomarker among structural neuroimaging with MRI, molecular neuroimaging with PET and cerebrospinal fluid analysis of amyloid or tau proteins.

**Issues Associated with a Lack of Diagnosis**

Some physicians and other health professionals do not feel that diagnosing AD is necessary due to the absence of any cure and the stress related to diagnosis. According to this school of thought, a diagnosis would not be too useful as it would lead to fear and emotional distress for patients, serving only to compound the patient’s misery of knowing they have the disease yet knowing there is no curative agent available. However, the counter-argument is that this assumption is not valid, as many patients exhibit a great desire for an early diagnosis, with up to 80% of older adults wishing to know as early as possible whether they have probable or definitive AD.12,13 A recent examination of short-term changes in depression and anxiety after receiving a dementia diagnosis, using a 15-item Geriatric Depression Scale and a 20-item ‘state’ version of the State–Trait Anxiety Inventory, noted that no significant changes in depression occurred in individuals or their companions, regardless of diagnostic outcome or dementia severity.14

The lack of a diagnosis of probable or definitive AD can have potentially deleterious consequences for the patient, as disease progression can lead to several problems, particularly in those with advanced stages of the disease with a low cognitive function score, e.g. an MMSE score <15. Such a low score has implications for the patient’s safety. Both the Réseau sur la maladie d’Alzheimer Français (REAL.FR) study15 and the Impact of Cholinergic Treatment Use (ICTUS) study16 observed that more than 19% of patients with AD live alone. This observation suggests a greater chance of patients with cognitive impairment experiencing medication compliance issues and/or making mistakes with medications. This in turn can lead to increased risks of side effects or aggravation of co-existing diseases when treatments are not taken. Memory loss is one of the most common symptoms of AD and has a significant impact on the daily routine of a patient. Memory loss will also affect a patient’s ability to manage personal and financial activities. AD could also have an impact on the nutritional intake of the affected person due to difficulties in carrying out shopping and cooking activities, which have been linked to a poor Instrumental Activities of Daily Living scale (IADL) score. AD could also have wider implications; for example, in cases where the patient is also a caregiver with responsibilities for a partner or family member who also has health issues, AD may have a negative impact on the provision of care. Advancing AD could also have a significant negative impact on the caregiver, as deteriorating disease leads to a decrease in cognitive function of the patient and increased dependence on the caregiver.

**Understanding the Importance of an Earlier Diagnosis**

Increasing evidence shows that AD progresses slowly during the early phase of the disease and that the disease evolves along a predictable pattern of progression in the brain,16 with the molecular pathomechanisms of AD becoming active many years before neurons start dying and clinical symptoms appear.17 Since there would be a lower burden of amyloid and hyperphosphorylated tau, little or no deterioration in cognitive function in the early stages of the disease and a slow rate of disease progression, an earlier diagnosis followed by symptomatic or disease-modifying therapy could potentially be an effective strategy to help maintain a good quality of life for patients, family members and caregivers. The most commonly used agents for early AD are the cholinesterase inhibitors, including donepezil, rivastigmine and galantamine, which have been shown to improve cognitive and global function in some patients.

The early diagnostic approach has also provided primary care physicians with an opportunity to offer early psychosocial support directly to individuals affected by AD. Psychosocial support can be offered to early-stage groups, and the opportunity to share experiences and increased social support have been reported among the benefits of such an approach.18 While there are few trained professionals and a lack of psychosocial support groups, data indicate that psychotherapy of early-stage individuals could help manage the disease and reduce depression,19 and such an approach should be considered in the future.

Patients with AD have low functional disability and relatively good cognitive function in the early stages. Therefore, these patients can be involved in treatment planning, expressing opinions and desires regarding how to improve and maintain quality of life.20 Indeed,
patients with early-stage AD are increasingly requesting involvement in future treatment planning. Among the cognitive domains, the level of awareness affects the efficacy of some interventions. As this cognitive function deteriorates with advancing disease, a diagnostic and interventional strategy could be beneficial if carried out quite early in the disease process, when the level of awareness is near normal. By contrast, if the diagnosis is not made at all or only when the patient experiences severe health problems, the patient would have various complications, for example aggression, agitation, delusions, hallucinations and weight loss. At this point, the family would be confused and would not be able to understand the patient’s condition or why the diagnosis was not made earlier. This could also cause problems for the physician; for instance, the family could blame or question the physician’s decision to make a diagnosis only when the patient’s health had significantly deteriorated.

Patients with AD, their family members and their care-givers can be placed under great emotional and financial burden due to the patient’s declining cognitive and functional abilities. The burden on family members and caregivers affects the deteriorating cognitive ability of the patient, often leads to the latter requiring formal LTC services, which can be costly to the patient and family members. Instead, if AD is diagnosed as early as possible, there would be a great chance of managing disease progression and reducing the symptoms, leading to either delayed or reduced need for entry into nursing homes and consequently cost savings for the patient and family members. Other benefits would include improved economic efficiency and better quality of life for the patient and the individuals supporting him or her. In one study, Monte Carlo cost-benefit analyses evaluated the costs and benefits of the early identification and treatment of AD patients. The analyses used LTC cost data from Wisconsin and data about the potential benefits of pharmacological and non-pharmacological therapies (e.g. care-giver support). The net benefits have been combined for the years when cases are identified at earlier stages, e.g. at an MMSE score of 28, and when drug therapy has been combined with a care-giver intervention programme. Additionally, mean net social benefits of US$94,000 were reported for 10,000 trials for a particular Monte Carlo analysis, assuming a drug treatment effect (MMSE/L) for a 70-year-old married woman with a starting MMSE score of 26. These analyses show that early detection of AD followed by pharmacological intervention and care-giver support results in large, positive net social benefits. These findings also indicate that the attitude of healthcare professionals towards AD will have to change, with physicians aiming to diagnose and treat AD as early as possible, paying particular attention to the oldest sufferers as they are most likely to experience the greatest problems and be the largest consumers of LTC services.

Conclusions
While some physicians and health professionals may be reluctant to diagnose AD, this lack of diagnosis can result in numerous problems related to the symptoms of disease, with advancing disease resulting in significant deterioration in clinical symptoms, dependence on caregivers and the need for professional LTC services. Diagnosing AD as early as possible will allow the opportunity to achieve a good quality of life for patients, family members and caregivers for a longer period of time. For all of these reasons, it is important to diagnose AD early in the course of the disease, regardless of the patient’s age. Once detected, AD can be managed by the medical staff, the patient and the family circle. The worst situation would be to handle impairment, suffering and end-of-life care for an unknown diagnosis. The GP has a special role in detecting and following up patients with AD, especially the oldest of the aged patients. A task force discussed the importance of an early diagnosis of AD at the world congress of the International Association of Gerontology and Geriatrics in July 2009. The speakers provided an update on biomarkers, imaging technologies and the usefulness of various early-stage diagnostic tools as part of therapeutic monitoring, and discussed neuroradiological biomarkers that could enable assessment of disease progression during clinical trials using new compounds that target amyloid protein or other lesions.