

SPREAD

Stroke Prevention And Educational Awareness Diffusion

2003

Italian Guidelines for Stroke Prevention and Management

Syntheses and Recommendations

Release of 4 March 2003

In collaboration with:

Associazione Italiana Fisioterapisti (AIFI)
Associazione Italiana di Neuroradiologia (AINR)
Associazione Nazionale Cardiologi Extraospedalieri (ANCE)
Associazione Nazionale Infermieri di Neuroscienze (ANIN)
Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO)
Federazione delle Associazioni dei Dirigenti Ospedalieri Internisti (FADOI)
Federazione Logopedisti Italiani (FLI)
Italian College of Applied Molecular Medicine (ICAMM)
Società Italiana di Angiologia e Patologia Vascolare (SIAPAV)
Società Italiana di Chirurgia Vascolare ed Endovascolare (SICVE)
Società Italiana di Cardiologia (SIC)
Società Italiana Cardiologia Ospedalità Accreditata (SICOA)
Società Italiana di Diabetologia (SID)
Società Italiana di Farmacologia (Sezione di Farmacologia Clinica) (SIF)
Società Italiana di Gerontologia e Geriatria (SIGG)
Società Italiana di Geriatria Ospedaliera (SIGO)
Società Italiana Ipertensione Arteriosa (SIIA)
Società Italiana Medicina di Famiglia (SIMEF)
Società Italiana di Medicina d'Emergenza-Urgenza (SIMEU)
Società Italiana di Medicina Fisica e Riabilitazione (SIMFER)
Società Italiana di Medicina Generale (SIMG)
Società Italiana di Medicina Interna (SIMI)
Società Italiana di Neurologia (SIN)
Società Italiana di Neurochirurgia (SINch)
Società Italiana di Neurosonologia ed Emodinamica Cerebrale (SINSEC)
Società Italiana di Nutrizione Umana (SINU)
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Società Nazionale di Aggiornamento Medico Interdisciplinare (SNAMID)
Scienze Neurologiche Ospedaliere (SNO)

and:

Associazione per la Lotta all'Ictus Cerebrale (ALICE)
Associazione per la Lotta alla Trombosi (ALT)

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Associazione Nazionale Cardiologi Extraospedalieri (ANCE)	<i>National Association of extra-Hospital Cardiologists</i>
Associazione Nazionale Infermieri di Neuroscienze (ANIN)	<i>National Association of Neuroscience Nurses</i>
Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO)	<i>National Association of Hospital Cardiology Physicians</i>
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Società Italiana di Diabetologia (SID)	<i>Italian Society of Diabetology</i>
Società Italiana di Farmacologia (Sezione di Farmacologia Clinica) (SIF)	<i>Italian Society of Pharmacology-Clinical Pharmacology Section</i>
Società Italiana di Gerontologia e Geriatria (SIGG)	<i>Italian Society of Gerontology and Geriatrics</i>
Società Italiana di Geriatria Ospedaliera (SIGO)	<i>Italian Society of Hospital Geriatrics</i>
Società Italiana Ipertensione Arteriosa (SIIA)	<i>Italian Society of Arterial Hypertension</i>
Società Italiana Medicina di Famiglia (SIMEF)	<i>Italian Society of Family Physicians</i>
Società Italiana di Medicina d'Emergenza-Urgenza (SIMEU)	<i>Italian Society of Medicine in Emergencies and Urgencies</i>
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INTRODUCTION

The development of the Italian Guidelines on Stroke has been a coordinate process, involving a multidisciplinary working group, denominated "SPREAD Collaboration" (Stroke PREvention and Awareness Diffusion), in which at present thirty-three different professional organisations and two patients associations are represented. The group was organised in operative subcommittees. Each subcommittee dealt with a different area covered by the guidelines and was composed of 5-10 experts in the specific field. Furthermore, a "scientific task force" and an editorial board were assigned to coordinate and review the texts progressively processed.

Since early 1998, when works officially started, three consecutive versions were released thanks to an intense multidisciplinary cooperation in the processing phase and in the consensus achievement. Most of the work and the communications occurred electronically through the limited-access section of an specifically set-up intranet. Plenary or single area meetings took place at crucial decisional points.

During the consecutive editions of the national forum "Stroke", held annually in Florence, the final versions of the guidelines were officially presented for comments and consensus by experts, nurses, physiotherapists, patients, and regional representatives.

Finally the ultimate versions were submitted for approval to the medical associations involved.

The guideline development was financially supported by an unconditional grant from Bayer Healthcare Italy. None of the participants to the working groups declared conflicts of interest.

In the first two versions of the guidelines (1999, 2001) the classification of the strength of evidence and the grades of recommendations were derived from what stated by the AHCP (Agency for Health Care Policy and Research, now AHRQ, Agency for Healthcare Research and Quality).

However some critical issues came out in the application of this methodology of weighing the available scientific evidence. The classification of the results from a randomised, controlled study (RCT) only as statistically "strong" or "weak" appeared unsatisfactory for the actual practice. It was necessary to consider the strength of the evidence, the methodological quality of the studies, the external validity, by applying a "considered judgment" on the whole amount of the data.

The direct applicability of the results of a study to the target population addressed by the guidelines was considered as well.

Accordingly a new methodology was developed by integrating the principles of the SIGN (Scottish Intercollegiate Guideline Network) with the statistical considerations on alpha and beta error size suggested by the CEBM (Centre for Evidence-Based Medicine) methodology (Tables 1 and 2).

Table 1. Levels of evidence

1++	High quality meta analyses without heterogeneity, systematic reviews of RCTs each with small confidence intervals (CI), or RCTs with very small CI and/or very small alpha and beta
1+	Well conducted meta analyses without clinically relevant heterogeneity, systematic reviews of RCTs, or RCTs with small CI and/or small alpha and beta
1-	Meta analyses with clinically relevant heterogeneity, systematic reviews of RCTs with large CI, or RCTs with large CI and/or alpha or beta
2++	High quality systematic reviews of case-control or cohort or studies. High quality case-control or cohort studies with very small CI and/or very small alpha and beta
2+	Well conducted case control or cohort studies with small CI and/or small alpha and beta
2-	Case control or cohort studies with large CI and/or large alpha or beta
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Table 2. Grades of recommendation

A	At least one meta analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; <i>or</i> A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 2++
D	Evidence level 3 or 4; <i>or</i> Extrapolated evidence from studies rated as 2+
Good Practice Point (*GPP)	Recommended best practice based on the clinical experience of the guideline development group, without research evidence

The aim of these guidelines is to provide knowledge and recommendations about the best management of acute stroke and the primary and secondary prevention of stroke in the clinical practice.

These guidelines are not only informative but also normative, though in a non-binding way.

The recommendations are judged valid when they:

- explicitly consider all the important steps of the clinical decision-making process and the relevant outcomes;
- identify the best evidence concerning stroke treatment and prevention, and critically evaluate its reliability;
- identify and take into account the preferences of the involved subjects concerning the outcomes of the decisions taken (including benefits, risks and costs).

The recommendations are relevant when they:

- intervene in situations of broad variability in the clinical practice;
- provide new evidence that may have specific impact on a current therapeutic conduct;
- concern the treatment of such a number of subjects that even small changes in the practice could have a strong impact on outcomes and on allocation of resources.

The ethical frame of these guidelines is based on four fundamental principles:

- beneficence;
- non-maleficence;
- autonomy;
- justice;

taking however into account, with equal dignity, the different ethical positions deriving from the unavoidable contrasts between ethics, economy and law, which also affect the model of the patient-doctor relationship.

At present, reliable evaluations of cost-effectiveness of the main treatments and procedures considered in these guidelines are not available in Italy. If such studies are performed it will be advisable also to consider the problems related to the estimation of costs:

- exclusion of important cost factors;
- inclusion of costs that are not surely attributable to the project;
- improper or incorrect cost estimation;
- inadequate actualisation of cost values;
- uncertainty of the estimates (sensitivity analysis);
- improper use of average costs;
- confusion and overlapping between costs and tariffs.

In any case, costs should be classified as direct, indirect or intangible (that compounded constitute the total cost), in relation to the measure of effectiveness and/or of benefit that is defined as appropriate.

Synthesis 1-1

Synthesis 1-2

Synthesis 1-3

Synthesis 1-4

Synthesis 1-5

Synthesis 1-6

METHODOLOGY**Synthesis 2–1**

These guidelines have been formulated following a multidisciplinary approach in order to be:

- applicable to the Italian setting;
- based on the best available research evidence;
- updated to the most recent scientific developments;
- propositional and flexible.

Synthesis 2–2

The sources of evidence to formulate these recommendations have been the Cochrane Database of Systematic Reviews and electronic medical literature databases (e.g. MEDLINE), as well as data from both Italian and international researches directly available to the experts involved in the guidelines formulation. Documented consensus on developing topics was also taken into account.

Synthesis 2–3

The recommendations are always explained by the scientific work-up which they derive from, in order to provide formative teaching to the reader. These guidelines in fact aim to help, not to replace, the clinical judgement necessary in each single case.

Synthesis 2–4

For each recommendation a formal consent was sought on:

- validity;
- reliability;
- clinical relevance;
- applicability;
- comprehensibility;
- flexibility;
- respect of persons.

Documented dissent is also reported.

Synthesis 2–5

For the developmental process and consensus achievement on these guidelines, electronic communications, general meetings or meetings involving the single area participants have been used, according to the specific decisional task.

Synthesis 2–6

In order to make these guidelines a practical tool, each recommendation has been formulated taking into account:

- flexibility;
- clearness;
- minimal intrusion into the clinical practice.

Synthesis 2–7

The conscious decision of not complying with a recommendation cannot be considered as a specific blame. Nevertheless, complying with the recommendations of a guideline is usually the most effective clinical behaviour.

Synthesis 2–8

These guidelines are being disseminated through:

- pamphlet for quick consultation of the main recommendations;
- summary of all recommendations for use in the daily clinical practice;
- comprehensive textbook containing all the scientific material produced;
- electronic version accessible via Internet

Synthesis 2–9

These guidelines will be tested by specialists and general physicians by applying them on a general population sample to evaluate their applicability.

EPIDEMIOLOGY

In Italy, stroke is the third cause of death (the seconds in some reports) after cardiovascular diseases and tumours. It causes 10%-12% of all deaths every year, and represents the main cause of disability.

In the Italian elderly population (age 65-84 years), stroke prevalence is 6.5%, slightly higher in men (7.4%) than women (5.9%).

Stroke incidence increases progressively with age, reaching the peak among people 85 years old and over. Therefore, 75% of all strokes affects subjects older than 65 years.

Ischaemic stroke is the most common kind of stroke (about 80%) whereas 15%-20% of all strokes are accounted for by cerebral haemorrhages, and 3% by subarachnoid haemorrhages.

Ischaemic stroke affects mostly people over 70 years of age and males; haemorrhagic stroke affects slightly younger people, more commonly males; subarachnoid haemorrhage affects mostly females with a mean age of 50 years.

In Italy about 194,000 strokes occur every year (data from general population on 2001), 80% of them are first-ever strokes (155,000) while 20% (39,000) are recurrent strokes.

In Italy, assuming a constant stroke incidence, and considering the progressive ageing of the population, about 207,000 strokes are expected to occur on 2008: 80% of them will be first-ever strokes and the remaining 20% will be recurrent strokes

In Italy, prevalent stroke cases are about 907,000 as estimated from the general population data on 2001.

In Italy, prevalent stroke cases are expected to be about 955,000 on 2008, assuming constant incidence and mortality rates.

Acute mortality (first 30 days) after stroke is 20%, while it reaches the 30% after one year. Haemorrhages (intracerebral and subarachnoid) show a higher acute mortality (30% and 40% respectively after a week; 50% and 45% after 1 month).

After one year following either an ischaemic stroke or a cerebral haemorrhage, about a third of patients remain severely disabled (i.e. totally dependent in the activities of daily living).

Synthesis 4-1

Synthesis 4-2

Synthesis 4-3

Synthesis 4-4

Synthesis 4-5

Synthesis 4-6

Synthesis 4-7

Synthesis 4-8

Synthesis 4-9

Synthesis 4-10

Synthesis 4-11

		DIAGNOSTIC WORK-UP
Synthesis 5–1		The identification of the pathophysiologic mechanism of a transient ischaemic attack (TIA) or a stroke has important prognostic and therapeutic implications. The diagnosis relies on both clinical and instrumental data.
Recommendation 5.1	Grade C	According to the World Health Organisation (WHO) definition, a TIA is characterised by the sudden development of signs and symptoms of focal cerebral or visual deficit of vascular origin lasting less than 24 hours. Such symptoms as isolated loss of consciousness, dizziness or vertigo, transient global amnesia, drop attack, generalised weakness, delirium or sphincteric incontinence are not specific enough for a definite diagnosis of TIA.
Recommendation 5.2	Grade D	The diagnosis of TIA or stroke is only clinical. Nevertheless the use of computed tomography (CT) or magnetic resonance imaging (MRI) is recommended to corroborate differential diagnosis with other pathologies that can mimic TIA or stroke.
Synthesis 5–2		The rupture of an arterial aneurysm is the cause of spontaneous subarachnoid haemorrhages in 80% of cases.
Recommendation 5.3	Grade D	A cranial CT or MRI is recommended to be performed as soon as possible from stroke onset to distinguish between ischaemic and haemorrhagic stroke and to choose the proper therapeutic approach.
Recommendation 5.4	Grade D	After a TIA or a stroke, an Holter ECG monitoring is recommended only when cardio-embolism is suspected or no other definite pathophysiologic mechanism is identified.
Recommendation 5.5	Grade D	After a TIA or a stroke, transthoracic echocardiography (TTE) is recommended only when a heart disease is clinically suspected.
Recommendation 5.6	Grade D	After a TIA or a stroke, when a cardioembolic mechanism is suspected, transesophageal echocardiography (TEE) is recommended in patients under 45 years of age with no evident causes of cerebral ischemia, or instrumental evidence of cerebrovascular disease, or major vascular risk factors.
Recommendation 5.7	Grade D	In patients with an isolated TIA, a brain CT is recommended to investigate the presence of an ischaemic brain lesion and its correspondence to the clinical presentation.
Synthesis 5–3		Leukoaraiosis cannot be considered as a specific marker of cerebrovascular disease, even if it is more frequently observed in patients with cerebrovascular risk factors, such as hypertension.
Synthesis 5–4		Magnetic resonance can detect silent cerebral infarcts that are associated with an increased risk of stroke.
Synthesis 5–5		In patients with previous TIA and/or stroke, MRI is more sensitive than CT to detect posterior infarcts or small brain lesions.
Synthesis 5–6		In patients with previous intracerebral haemorrhage, accumulation of haemosiderin is a permanent marker of previous bleeding at brain MRI.
Synthesis 5–7		Cerebral angiography is indicated in children or young patients with ischaemic stroke because at these ages the cause is often a cerebral vasculitis.
Synthesis 5–8		In expert centres where intra-arterial procedures are successfully performed, angiography is indicated to confirm the suspicion of posterior circulation vessel (vertebral or basilar arteries) occlusion preliminary to intervention.
Synthesis 5–9		When suspecting a cerebral vasculitis or a non-atherosclerotic disease of extracranial arteries (dissections, vascular malformations) angiography has the highest diagnostic validity compared to other non-invasive techniques.
Recommendation 5.8	Grade D	Angiography of intracranial vessels is the gold standard for the study of cerebral aneurysms and it is indicated in patients with subarachnoid haemorrhage who are candidates to surgery or to endovascular treatment.
Raccomandazione 5.9	Grade D	Electroencephalography (EEG) is recommended in patients who are suspected to have an epileptic cause of their stroke-like symptoms.
Recommendation 5.10	Grade D	In patients with TIA or recent stroke, ultrasonography (US) studies of supra-aortic vessels is recommended among investigations aimed at defining the mechanisms of ischemia.
Synthesis 5–10		The degree of carotid stenosis in the perspective of a surgical or an endovascular treatment, should be primarily estimated using non-invasive techniques (Duplex US, MRA, CT angiography). Angiography should be performed when the results of non-invasive examinations are discordant, or a significant atherosclerotic disease of intracranial arteries is suspected, especially in vertebrobasilar arteries, or when MRA or CT angiography give technically poor images.

Duplex US examination of supra-aortic vessels can replace angiography, for selecting patients with carotid stenosis to be submitted to endarterectomy, only if it is integrated with non-invasive studies (MRA, CT angiography) of intracranial vessels. The whole diagnostic procedure has to be validated in each single centre against angiography before being used routinely.

In patients who are undergoing major cardiovascular surgery, Duplex US examination of supra-aortic vessels **is recommended** to look for possible carotid artery stenoses and therefore to evaluate the risk of ischaemic cerebral complications.

After carotid endarterectomy (CEA), Duplex US examination of supra-aortic vessels **is recommended**, at 3 and 9 months and every year thereafter, to monitor recurrent stenosis.

Duplex US examination of supra-aortic vessels is recommended in asymptomatic subjects with:

- a non-cardiogenic carotid bruit;
- a high probability to have carotid stenosis (e.g. subjects with peripheral artery disease or well-documented coronary artery disease, or subjects over 65 years with multiple vascular risk factors).

Lacking conclusive evidence, the prognostic value of ultrasound characteristics (echogenicity or lucency) of carotid plaques is undefined.

Transcranial Doppler is a complementary examination in patients with a recent TIA or stroke. It may provide additional information on patency of cerebral vessels, recanalization and collateral pathways.

Transcranial Doppler is a complementary examination in patients who are undergoing carotid endarterectomy, helping in pre-operative evaluation and intraoperative monitoring of flow in the operated artery territory.

Transcranial Doppler can substitute transesophageal echocardiography to detect a right-to-left cardiac shunt.

Transcranial Doppler **is recommended** in patients with subarachnoid haemorrhage to detect the possible occurrence of vasospasm.

In patients who are candidates to carotid endarterectomy (CEA), coronary angiography **is recommended** when there is clinical or non-invasive instrumental evidence of coronary artery disease at high risk of myocardial ischemia.

In patients who are candidates to carotid endarterectomy (CEA) and have an associated severe coronary artery disease, it **is recommended** to consider a possible coronary revascularization procedure, carrying out the two interventions either separately (treating first the symptomatic district), or in combination with CEA.

Recommendation 5.11 Grade B

Recommendation 5.12 Grade D

Recommendation 5.13 Grade D

Recommendation 5.14 Grade D

Synthesis 5–11

Recommendation 5.15 Grade D

Recommendation 5.16 Grade D

Recommendation 5.17 Grade D

Recommendation 5.18 Grade D

Recommendation 5.19 Grade D

Recommendation 5.20 Grade D

RISK FACTORSSynthesis 6–1

Epidemiological studies have identified several risk factors for stroke. Some factors (i.e. age) cannot be modified; nevertheless they contribute to define the risk classes. Other factors can be modified through pharmacological or non-pharmacological intervention, and their identification is crucial to primary and secondary stroke prevention.

Synthesis 6–2 a

Well-documented modifiable risk factors for stroke are:

- arterial hypertension;
- some heart diseases (particularly atrial fibrillation);
- diabetes mellitus;
- hyperhomocystinaemia;
- left ventricular hypertrophy;
- carotid stenosis;
- cigarette smoking.

Synthesis 6–2 b

Transient ischaemic attack is a well-documented risk factor for stroke.

Synthesis 6–3 a

Other probable risk factors for stroke, which have not been completely documented so far as independent risk factors, include:

- dyslipidaemia;
- some heart diseases (patent foramen ovale, septal aneurysm);
- plaques of the aortic arch;
- use of oral contraceptives;
- alcohol abuse;
- low physical activity;
- migraine;
- antiphospholipid antibodies;
- haemostasis factors;
- infections;
- drug use.

Synthesis 6–3 b

Hypercholesterolemia is the best documented modifiable risk factor for coronary artery disease, but its association with stroke is incompletely defined.

Synthesis 6–4

Age is the most important risk factor for stroke. The incidence of stroke increases with age, and after 55 years it doubles for every decade. The majority of strokes occur in subjects over 65 years.

Synthesis 6–5

Predisposition to stroke may be inherited, although the role of genetic factors in the pathogenesis of stroke is still undefined.

Synthesis 6–6

The interaction of the different risk factors is factorial rather than simply additive, and the risk of death due to stroke increases with the number of factors, even if the individual attributable risk is limited.

PRIMARY PREVENTION

Counselling and promotion of correct life-styles **are recommended** to decrease stroke incidence and mortality, in the entire population but especially in subjects at high risk of vascular diseases.

Smoking cessation decreases the risk of stroke. It **is recommended** for all smokers independently of age and amount of smoking.

It **is recommended** to limit the alcohol intake to two glasses of wine (or an equivalent amount of alcohol) per day in men and to one in women.

A moderate physical activity (fast walking at 10-12 minutes per kilometre) **is recommended** for at least 30 minutes in most days of a week, because it is associated with decreased stroke incidence.

It is possible to decrease the risk of stroke by means of dietary modification.

Some nutrients are associated with an increased risk of ischaemic stroke:

- sodium intake: a positive association with higher blood pressure is reported. It could also play a direct role on stroke pathogenesis.
- saturated fats: high consumption is associated with risk factors correlated with stroke such as hyperlipidaemia, obesity, and hypertension.

Some nutrients have been reported to have a protective effect:

- *unsaturated fats*: the protective effect is documented for the intake of monounsaturated (oleic acid) as well as of polyunsaturated (linoleic acid and omega-3) fatty acids, and it is potentiated in diets low in saturated fats.
- *intake of fibres*: a positive effect is suggested in particular in hypertensive males, but further evidence is needed.
- *potassium, magnesium and calcium*: an inverse correlation is documented between the intake of those minerals and the risk of stroke, attributable to an interaction with blood pressure.
- *antioxidant compounds*: an equilibrated antioxidant intake has a protective effect that is mostly related to the consumption of vitamin C and E, and of beta-carotene. A dietary supplementation does not seem to modify the risk profile.
- *folic acid, vitamin B₆ and vitamin B₁₂*: an adequate dietary intake may exert a protective effect, possibly related to the reduction of homocysteinaemia. A dietary supplementation is advisable in case of hyperhomocysteinaemia.

In the general population it **is recommended** to achieve the following specific nutritional targets:

salt intake ≤ 6 g/day (2.4 g of sodium). Salty food and adding salt to the food while eating should be avoided.

low consumption of dietary animal fats in favour of vegetable fats (in particular olive oil) and use of preferably raw seasonings.

consumption of fish 2-3 times per week (at least 400 g overall) as a source of polyunsaturated fatty acids.

several servings of fruit and vegetables each day (at least 400-500 g/day) and regular consumption of whole grains and legumes (rich in fibre, vitamins, folic acid and minerals).

regular consumption of milk and dairy products, choosing low-fat products.

The treatment of arterial hypertension **is recommended** in all hypertensive subjects independently of age, severity of hypertension and global cardiovascular risk, because it decreases the risk of stroke. The target indicated by the ESH-ECS guidelines for 2003 is a blood pressure <130 and <80 mm Hg in diabetic patients, and at least <140 and <90 mm Hg – or definitely lower if tolerated – in all other hypertensive subjects.

In elderly subjects with isolated systolic hypertension, an antihypertensive treatment **is recommended**, preferring the use of diuretics or long-acting dihydropyridine Ca-antagonists.

In hypertensive patients with left ventricular hypertrophy, the use of antihypertensive agents that blocks the renin-angiotensin system, such as losartan (demonstrated in one study to be superior to atenolol also for stroke prevention) **is recommended**.

In patients with an high thrombotic risk (presence of coronary artery disease, peripheral artery disease, or diabetes mellitus associated with another vascular risk factor such as hypertension, hypercholesterolaemia, low HDL-cholesterol, cigarette smoking or microalbuminuria), for the primary prevention of stroke it **is recommended** to use ramipril at the 10 mg/day dosage.

Recommendation 7.1 Grade D

Recommendation 7.2 Grade D

Recommendation 7.3 Grade D

Recommendation 7.4 Grade D

Synthesis 7-1

Recommendation 7.5

a (Grade D)

b (Grade D)

c (Grade D)

d (Grade C)

e (Grade D)

Recommendation 7.6 a Grade A

Recommendation 7.6 b Grade A

Recommendation 7.6 c Grade C

Recommendation 7.6 d Grade B

Recommendation 7.7	Grade B	Oral anticoagulants, maintaining the international normalised ratio (INR) in the 2 to 3 range, are recommended for patients with atrial fibrillation and valvular heart disease, independently of the presence of other risk factors.
Recommendation 7.8 a	Grade D	In patients with non-valvular atrial fibrillation, cardioversion is recommended as the first therapeutic approach.
Recommendation 7.8 b	Grade A	In patients aged 65-75 years with non-valvular atrial fibrillation, oral anticoagulant therapy, maintaining the INR at 2-3, is recommended in absence of haemorrhagic risks.
Recommendation 7.8 c	Grade A	In patients with non-valvular atrial fibrillation, age over 75 years, and additional risk factors for thromboembolism (e.g. diabetes, arterial hypertension, heart failure, left atrial dilatation, left ventricular dysfunction), long term oral anticoagulation therapy (INR range 2-3) is recommended , evaluating carefully each individual case and taking into account the increased hemorrhagic risk [especially intracranial] of elderly people.
Recommendation 7.8 d	Grade A	Although less effective, aspirin (ASA) therapy (325 mg per day) is recommended as an alternative to anticoagulant therapy in non-valvular atrial fibrillation for: <ul style="list-style-type: none"> • patients over 65 years with contraindications to oral anti-coagulants; • patients over 75 years with higher hemorrhagic than thrombo-embolic risk; • patients with anticipated poor compliance with the anticoagulant therapy or difficult access to reliable therapy-monitoring facilities.
Recommendation 7.8 e	Grade A	In patients under 65 years with isolated non-valvular atrial fibrillation, no prophylactic treatment is recommended because the embolic risk is low. In presence of additional embolic risks, these must be evaluated in the individual case to decide between ASA and oral anticoagulant therapy.
Recommendation 7.9	Grade C	Long term oral anticoagulation therapy is recommended in patients with mechanical valvular prosthesis (INR range 2.5-3.5, and INR range 3-4 in case of ball valve or caged disk valve).
Recommendation 7.10 a	Grade B	In patients with coronary artery disease, the use of statins for the treatment of hypercholesterolemia is recommended for the primary prevention of stroke.
Recommendation 7.10 b	Grade A	In patients at high risk of vascular disease, therapy with simvastatin (40 mg per day) is recommended for the primary prevention of stroke.
Recommendation 7.10 c	Grade D	In hypertensive patients with at least three additional risk factors, therapy with atorvastatin (10 mg per day) is recommended for the primary prevention of stroke.
Recommendation 7.11 a	Grade D	The diagnosis and treatment of diabetes mellitus is recommended as a possible contribution to stroke risk reduction.
Recommendation 7.11 b	Grade A	In diabetic patients ≥ 30 years old with at least one additional risk factor, therapy with aspirin is recommended for the primary prevention of stroke
Recommendation 7.12	Grade C	In patients with antiphospholipid antibodies, anti-thrombotic therapy is recommended only for those with a history of thrombotic events
Recommendation 7.13	*GPP	Although plaques of the aortic arch may be a risk factor for stroke, at present their treatment with anti-thrombotic agents is not recommended because the risk-to-benefit evidence is still inconclusive

Synthesis 8–2	Acute stroke is a medical emergency that deserves immediate hospitalisation, as stated in the Helsingborg Declaration and in several guidelines. All patients suffering cerebral vascular events should be admitted to a hospital to undergo a quick and accurate diagnostic work-up, and to monitor and treat possible complications.
Synthesis 8–3	<p>There are three possible categories of stroke care organisation:</p> <ol style="list-style-type: none"> 1. the stroke unit admitting only acute cases with very short hospitalisation periods and rapid transfers; 2. the stroke unit combining assistance during the acute phase with rehabilitation, in which discharge occurs with a rehabilitation and secondary prevention programme; 3. the purely rehabilitative stroke unit, which only receives patients with stroke sequels and stabilised. <p>Hospitals without a stroke unit may be equipped with a mobile stroke team formed by a physician and nurses available on call 24/24 hours.</p>
Synthesis 8–4	<p>The hospital receiving patients with acute stroke should ensure:</p> <ul style="list-style-type: none"> • computed tomography 24/24 hours; • laboratory for blood chemistry, including coagulation tests, 24/24 hours; • immediate cardiological and neurological evaluation. <p>US examination of intra- and extracranial vessels and echocardiography should be possible. Anyway the minimum level of stroke care should consist of:</p> <ul style="list-style-type: none"> • CT scan within 24 hours, • immediate evaluation by a physician with expertise in stroke care, • rehabilitative evaluation within 24-48 hours.
Synthesis 8–5	<p>A stroke unit consists of a hospital unit or part of a hospital unit with 4-16 beds, in which a multidisciplinary team of nurses, physiotherapists, occupational therapists, speech and language therapists and physicians, expert in cerebrovascular diseases, is dedicated to stroke care.</p> <p>The aspects qualifying the stroke unit are: the multidisciplinary of the team, the integrated medical and rehabilitative approach, the continuing medical education of the team and the education of patients and relatives.</p>
Synthesis 8–6	<p>A second-level hospital should administer the routine blood exams and the neuroimaging study (CT and/or MRI) within 60 minutes from admission of a stroke patient and it should perform the intravenous or the intra-arterial thrombolysis within 3 hours from stroke onset. Neurosurgical evaluation should be available within a maximum of 2 hours.</p>
Synthesis 8–7	<p>In the hospitals that have a stroke team but are not equipped to perform the thrombolysis, an optimal management of a stroke patient should be aimed to define the diagnosis (even using telemedicine), and to maintain stable clinical conditions.</p> <p>A fast transfer to a second-level hospital should be available for selected cases.</p>

ACUTE STROKE: HOSPITAL ADMISSION (DIAGNOSTIC PROCEDURES)

A stroke victim should rapidly be assessed after hospitalisation, by means of a general examination and a comprehensive neurological and cardiological evaluation.

An early and standardised neurological evaluation is recommended in the setting of a qualitatively adequate management of acute stroke.

The aims of an early clinical evaluation are:

- determine the time of stroke onset as accurately as possible (within a 30 min range);
- confirm the cerebrovascular nature of the neurological deficits;
- measure the severity of the neurological impairment (using clinical scales such as the National Institutes of Health Stroke Scale or the Scandinavian Stroke Scale) for prognostic purposes and for monitoring the clinical course;
- define the arterial territory (carotid or vertebrobasilar) for diagnostic, prognostic and therapeutic purposes;
- identify the possible pathogenetic subtype;
- forecast the outcome;
- identify the risk of medical or neurological complications for an early preventive or therapeutic approach;
- start the most appropriate treatment as timely as possible.

It is recommended that the neurological assessment is performed by a neurologist or alternatively by a physician expert in stroke evaluation and care.

The clinical definition of the involved vascular territory is recommended for its practical implications, including the diagnostic work up, the correlation with the results of neuroimaging, the identification of the mechanism, the prognostic assessment and the therapeutic decisions.

The diagnosis of stroke may be probable or possible. Two concurrent probable diagnosis may be hypothesised if the criteria for each of them are satisfied.

On admission to hospital of a suspected stroke victim the following blood exams are recommended: complete blood count, serum glucose, serum electrolytes, creatinine, BUN, serum total protein, bilirubin, transaminases, coagulation tests.

In patients with acute stroke, the lumbar puncture is recommended only when a subarachnoid haemorrhage is clinically suspected and the CT scan is negative.

The chest radiography is always suggested early after the hospital admission for the evaluation of heart failure, aspiration pneumonia or other possible cardiological or pulmonary early complications.

The electrocardiogram is recommended in all suspected stroke victims who are admitted to an Emergency Room.

A non-contrast CT scan is recommended in the emergency care (within 6 h in the second-level centres) and however not later than 24 h from stroke onset:

- to allow the differential diagnosis between ischaemic and haemorrhagic stroke, and with non-cerebrovascular lesions;
- to detect possible early signs of infarct.

The use of adequate technical parameters and positioning criteria is recommended for CT scan assessment of acute stroke.

In the emergency phase, MRI does not provide more information than CT scan. The diffusion- and perfusion-weighted sequences may be helpful for a more accurate pathogenetic and prognostic evaluation and for a better selection of patients who are candidates to i.v. or i.a. thrombolysis.

The diffusion- and perfusion-weighted MRI may be helpful in trials on new treatments.

When deciding to acquire new MRI machines, it should be taken into account the possibility to implement MRI diffusion, perfusion and spectroscopy techniques.

Digital subtraction angiography is recommended in the acute stroke only if pre-procedural to an intra-arterial thrombolysis approach. Otherwise the study of arterial occlusion may be obtained by means of MRA or CTA.

After the acute phase, the neuroimaging control may be performed by either CT scan or MRI. The MRI is more accurate in case of lacunar or brainstem infarct.

The repetition of non-contrast CT scan is recommended within 48 h and anyhow not later than 7 days from stroke onset. It is particularly recommended when stroke is severe or progressing, or the diagnosis of stroke is uncertain.

Synthesis 9-1

Recommendation 9.1 Grade D

Synthesis 9-2

Recommendation 9.2 Grade D

Recommendation 9.3 Grade D

Synthesis 9-3

Recommendation 9.4 Grade D

Recommendation 9.5 Grade D

Synthesis 9-4

Recommendation 9.6 Grade D

Recommendation 9.7 Grade D

Recommendation 9.8 *GPP

Synthesis 9-5

Synthesis 9-6

Synthesis 9-7

Recommendation 9.9 Grade D

Synthesis 9-8

Recommendation 9.10 Grade D

Synthesis 9–9

Soon after hospitalisation, ultrasound studies of cerebral vessels and echocardiography are useful for an early definition of pathogenic subtypes, of thromboembolic risk and for urgent therapeutic decisions. However their execution in this phase should be decided based on local facilities and following the indication in the specific case. In a subsequent phase, such studies have to be performed following the indications given in chapter 5.

Synthesis 9–10

Non-invasive TCD, MRA and CTA studies that evaluate the patency of cerebral vessels are helpful for establishing the site and severity of the arterial occlusion and for an adequate selection of potential candidates to thrombolysis (especially for the intra-arterial approach). At present, however, their use appears restricted to high-level centres.

ACUTE STROKE: HOSPITAL ADMISSION (TREATMENT)

Intravenous administration of streptokinase is not recommended.

The treatment with intravenous r-tPA (0.9 mg/kg, maximum 90 mg, with 10% of the dose given as a bolus followed by an infusion lasting 60 min) **is recommended** within 3 h of onset of ischaemic stroke.

* the panel partially disagreed on the strength of the recommendation (grade B instead of A) after considering what reported in literature about some methodological weaknesses of the NINDS study.

The benefit from the use of intravenous r-tPA for acute ischaemic stroke beyond 3 h after onset of the symptoms is smaller, but present up to 4.5 h. When r-tPA is administered between 4.5 and 6 h of stroke onset, only a statistically non-significant trend towards effectiveness is obtained.

An ongoing randomised controlled trial, denominated IST III, is estimating in a large population of patients with acute ischaemic stroke the risk-to-benefit ratio of the administration of r-tPA within 6 h of onset.

The thrombolysis should be performed in selected centres that are appropriately equipped to carry out the treatment within the due time limits and have the facilities for a close neurological and blood pressure monitoring during the 24 hours after treatment.

The selection of patients to be submitted to systemic thrombolysis should be accurate and inclusion/exclusion criteria should be carefully respected in order to optimise the risk-to-benefit ratio of the treatment.

The intravenous thrombolysis with r-tPA within 3 h is approved as a treatment of ischaemic stroke in USA, Canada and South America, and conditionally in Europe. The condition for approval is that, during the three years following approval, it is administered within 3 h of stroke onset in a phase-IV study denominated Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST), and within a time window of 3-4 h in a new randomised placebo-controlled study denominated ECASS III.

Intra-arterial thrombolysis is recommended for treatment of acute middle cerebral artery occlusion within 6 h of stroke onset.

Intra-arterial or intravenous thrombolysis are the recommended treatment of basilar artery occlusion within 6 h of stroke onset and in centres with expertise in interventional neuroradiology.

In patients with venous sinus thrombosis, when intravenous heparin therapy is ineffective, thrombolysis may be an optional treatment.

Ancrod is not recommended for the treatment of acute stroke.

Aspirin (160-300 mg per day) is recommended in all patients with acute stroke unless anticoagulant therapy or thrombolysis are indicated.

According to the SPREAD group the best aspirin dose in the acute stroke phase is 300 mg/daily.

The general use of unfractionated heparin, low molecular weight heparin and heparinoids **is not recommended** for the treatment of acute ischaemic stroke.

Anticoagulant therapy with intravenous heparin **is the recommended** treatment of large artery dissection and in patients with sub-occlusive carotid stenosis prior to surgery.

Anticoagulant therapy with intravenous heparin **is recommended** for the treatment of venous sinus thrombosis.

The use of neuroprotective drugs **is not recommended** for the treatment of acute ischaemic stroke.

Corticosteroids are not recommended for the treatment of acute ischaemic stroke.

Osmotherapy (mannitol, glycerol) is not recommended for the general treatment of acute ischaemic stroke. For the treatment of life-threatening brain oedema after stroke see recommendation 11.34 b.

The choice of the antithrombotic agent for early secondary prevention of stroke should be made according to the pathogenetic subtype of stroke (to be determined within 48 h of onset), to the severity of stroke, and to the potential patient's compliance with the treatment.

In patients with non-valvular atrial fibrillation, oral anticoagulation is recommended with a target INR between 2.0 and 3.0.

Recommendation 10.1 Grade A

Recommendation 10.2 Grade A

Synthesis 10-1

Synthesis 10-2

Synthesis 10-3

Synthesis 10-4

Recommendation 10.3 Grade D

Recommendation 10.4 Grade D

Synthesis 10-5

Recommendation 10.5 Grade C

Recommendation 10.6 Grade A

*GPP

Recommendation 10.7 Grade A

Recommendation 10.8 Grade D

Recommendation 10.9 Grade D

Recommendation 10.10 a Grade A

Recommendation 10.10 b Grade A

Recommendation 10.10 c Grade A

Synthesis 10-6

Recommendation 10.11a Grade B

Recommendation 10.11b Grade D	In patients with other cardio-embolic sources and an high risk of early stroke recurrence, the administration of full-dose i.v. heparin (target PTT ratio 1.5-2.5) followed by oral anticoagulation (target INR between 2.0 and 3.0 in heart valvular diseases with or without AF, and between 2.5 and 3.5 in presence of mechanical prosthetic valves) is recommended .
Recommendation 10.12 Grade D	In patients with any type of cardioembolic stroke, with the exception of those with high risk of recurrent embolism, and with a large infarct on the 48-h CT scan, a 2-week delay is recommended before starting anticoagulation, to avoid potential cerebral haemorrhagic complications. If on the CT scan the brain infarct is less than 30% of the involved hemisphere, and there is no haemorrhage, the treatment can be started earlier (48 hours).
Synthesis 10-7	If early (within 6 h of onset) CT signs of infarct are absent or smaller than 30% of the involved hemisphere, anticoagulation may be started immediately (a repeat CT scan within 48 h is needed to exclude delayed bleeding).
Synthesis 10-8	In patients with non-valvular AF, tranoesophageal echocardiography may reveal high cardio-embolic risk conditions such as left ventricular thrombus, dense spontaneous echo contrast, decreased flow velocity in the left atrial appendage, atheroma of the aortic arch. These patients should be considered at high risk of early re-embolism, but at present there is no evidence from randomised studies about the best anticoagulation approach (type of agent and timing).
Recommendation 10.13 Grade B	In patients with cardio-embolic stroke unable to receive oral anticoagulants, aspirin (160-300 mg per day) is recommended for the early secondary prevention of stroke.
Recommendation 10.14 Grade D	In patients with cardio-embolic stroke while on oral anticoagulation for atrial fibrillation and with INR values in the optimal range, anticoagulation therapy should be performed according to recommendation 10.12.
Recommendation 10.15 Grade D	In patients presenting with cardio-embolic stroke who have a prosthetic heart valve and are being treated with an adequate anticoagulation regimen, the supplementation of oral anticoagulation with an antiplatelet therapy is recommended .
Synthesis 10-9	In patients with acute stroke and a patent foramen ovale, therapeutic choices for secondary prevention are the same as those recommended for long-term therapy (see recommendation 12.12 a, b, c), and timing is that indicated in recommendation 10.12 and synthesis 10.7.
Recommendation 10.16 Grade A	In patients with stroke secondary to atherothrombosis of extracranial vessels who were not on antithrombotic therapy, aspirin (160-300 mg per day) is the recommended treatment.
Recommendation 10.17 Grade D	In patients with stroke secondary to atherothrombosis of extracranial vessels who have a recurrent event while on aspirin treatment, ticlopidine (250 mg bid, assessing blood cells count twice monthly for the first 3 months) or clopidogrel (75 mg per day), or dipyridamole slow release (200 mg bid) combined with aspirin (25 mg bid) are recommended .
Recommendation 10.18 Grade D	In patients with stroke secondary to atherothrombosis of extracranial vessels who have recurrent vascular events in spite of adequate anti-platelet therapy, oral anticoagulation (INR 2.0-3.0) is recommended .
Synthesis 10-10	There is no consistent evidence about the effectiveness of antithrombotic versus anticoagulation therapy in patients with aortic atheroma. On a theoretical basis they should be treated like those with atherothrombosis of extracranial arteries, but data reported in the literature are in favour of anticoagulation.
Synthesis 10-11	In patients with lacunar stroke, secondary prevention treatment should be decided after investigating all potential causes of stroke, including atherothrombosis and cardio-embolism.
Recommendation 10.19 Grade B	In patients at high risk of deep venous thrombosis (DVT) (i.e. presenting with plegic limbs, or reduced consciousness, or obesity or previous lower-limb venous diseases) prophylaxis with subcutaneous low-dose heparin (5000 i.u. twice daily) or low-molecular-weight heparins is recommended starting since hospital admission.
Synthesis 10-12	In patients at low risk of DVT, systematic prophylaxis with heparin has an unfavourable risk-to-benefit ratio considering the risk of intra- and extra-cerebral haemorrhagic complications.
Recommendation 10.20 Grade D	Early mobilisation and graded compression stockings as well as intermittent pneumatic compression are recommended for DVT prevention in combination with anticoagulation or as an alternative when anticoagulation is contra-indicated.
Recommendation 10.21 Grade D	Currently there is no evidence supporting treatment of progressing stroke patients with anticoagulation, unless high-grade carotid or basilar stenosis or basilar occlusion is documented.

For the prevention and treatment of progressing stroke, monitoring and adequate treatment of hyperthermia, hyperglycaemia and brain oedema are advisable.

During the first 15 days of treatment with heparin, regular monitoring of platelet count is recommended.

Immediate cessation of treatment with heparin **is recommended** in case of heparin-induced thrombocytopenia (proven or suspected).

In patients with heparin-induced thrombocytopenia, oral anticoagulation **is not recommended** as an alternative.

In patients who were already on adequate oral anticoagulation, the continuation of oral anticoagulants **is recommended** after cessation of heparin.

In patients with heparin-induced thrombocytopenia, therapy with hirudin, or dermatan sulphate, or danaparoid, or thrombolytic agents **is the recommended** alternative treatment. Oral anticoagulation may be started as soon as the platelet count recovers.

Surgical management of intracerebral haemorrhage **is recommended** in patients with:

- cerebellar haemorrhage larger than 3 cm and neurological deterioration or signs of brainstem compression and hydrocephalus;
- moderate to large lobar haemorrhage ($\geq 50 \text{ cm}^3$), with progressive neurological deterioration;
- intracerebral haemorrhage due to surgically-accessible aneurysms or arteriovenous malformations.

Surgical management of intracerebral haemorrhage **is not recommended** in patients with:

- small haemorrhage ($< 10 \text{ cm}^3$) or minimal neurological deficits (to be treated medically);
- $\text{GCS} \leq 4$ (owing to high mortality);
- intracerebral haemorrhage due to non surgically-accessible aneurysms or arteriovenous malformations

Currently there is no evidence or consensus about the surgical management of basal ganglia haemorrhage typical of hypertensive patients.

In patients with acute stroke, high grade symptomatic stenosis and crescendo TIAs or progressing stroke, the carotid endarterectomy (CEA) is recommended, in expert centres with perioperative complication rate of less than 3%, unless:

- a severe brain oedema and/or a large infarct or haemorrhage are present;
- a severe alteration of consciousness or of vital functions is present.

- a. Risk models ought to be employed to select the patients for the emergency CEA,
- b. Currently there is no evidence on the risk/benefit ratio of the emergency CEA in patients with progressing or acute (within 6 h) stroke even if associated with critical stenosis or acute carotid thrombosis.

Synthesis 10–13

Recommendation 10.22 Grade C

Recommendation 10.23 Grade D

Recommendation 10.24 Grade D

Recommendation 10.25 Grade D

Recommendation 10.26

a (Grade D)

b (Grade D)

c (Grade D)

Recommendation 10.27

a (Grade D)

b (Grade D)

c (Grade D)

Synthesis 10–14

Recommendation 10.28 Grade D

Synthesis 10–15

ACUTE STROKE: MONITORING AND COMPLICATIONS IN THE STEADY-STATE

Recommendation 11.1	Grade D	During the first 48 h after stroke onset, monitoring of the vital functions and neurological status is recommended . This should continue in case of clinical instability.
Recommendation 11.2	Grade D	During the first 48 h after stroke onset, on-line ECG monitoring is recommended , where feasible, in patients with: medical history of heart disease and/or arrhythmias, unstable blood pressure, clinical signs of heart failure, abnormal baseline ECG and infarcts involving the deep middle cerebral artery territories, especially insular cortex. In case of clinical instability, the monitoring should proceed beyond 48 h. Where the instrumental monitoring is not feasible, repeated ECGs are recommended during the first 24 h.
Recommendation 11.3	Grade D	In case of clinical signs of heart failure, the early execution of a transthoracic echocardiography is recommended .
Recommendation 11.4	Grade D	In patients with moderate-to-severe stroke, oxygenation monitoring is recommended at least during the first 24 h from onset. In case of respiratory abnormalities this should continue as long as the respiratory pattern recovers.
Recommendation 11.5	Grade D	Routine oxygen administration is not recommended in patients with acute stroke.
Recommendation 11.6	Grade D	Oxygen administration is recommended in case of hypoxaemia (blood gas analysis or O ₂ saturation <92% at pulse oxymetry).
Recommendation 11.7	Grade D	In case of moderate hypoxaemia without respiratory abnormalities, the administration of oxygen 2-4 litres per minute is recommended . Oxygen administration should start with high concentrations to be progressively reduced according to O _{2sat} values.
Recommendation 11.8	Grade D	For the emergency treatment of blood pressure in patients with acute ischaemic stroke the following algorithm is recommended : (from <i>Stroke Coding Guides of the American Academy of Neurology</i> , http://www.stroke-site.org/guidelines/stroke_coding.html ; February 2003, modified): <ol style="list-style-type: none"> 1. Blood pressure obtained by automatic sphygmomanometer should be correlated with a manual blood pressure cuff reading. 2. If diastolic blood pressure >140 mm Hg occurs on two readings 5 minutes apart, then start a continuous IV infusion of an antihypertensive agent such as sodium nitroprusside (0.5-1.0 mg/kg/min). Patients who fall into this category are not candidates for t-PA therapy even if other inclusion criteria are met. 3. If systolic blood pressure is >220 mm Hg or diastolic blood pressure is 121-140 mm Hg or mean arterial blood pressure is >130 mm Hg on two readings 20 minutes apart, then give an easily titratable antihypertensive medication such as labetalol at 10 mg IV over 1-2 minutes. The labetalol dose may be repeated or doubled every 10-20 minutes until a cumulative dose of 300 mg has been administered via this mini-bolus technique. After the initial dosing schedule, labetalol doses may be administered every 6-8 hours as needed. Labetalol is usually avoided in patients with asthma, cardiac failure, or severe cardiac conduction abnormalities. Patients who require more than two doses of labetalol or other antihypertensive agents to decrease blood pressure to <185 mm Hg systolic or 110 mm Hg diastolic are generally not candidates for thrombolytic therapy even if other criteria are met. 4. If systolic blood pressure is 185-220 mm Hg or diastolic blood pressure is 105-120 mm Hg, emergency therapy should be deferred in the absence of left ventricular failure, aortic dissection, or acute myocardial ischemia. Patients who are potential candidates for t-PA therapy, but who have persistent elevations in systolic blood pressure of >185 mm Hg or diastolic pressure of >110 mm Hg may be treated with small doses of IV antihypertensive medication to maintain the blood pressure just below these limits. However, more than two doses of an antihypertensive agent to lower the blood pressure below these limits is a relative contraindication for thrombolytic therapy and should be discouraged. 5. The use of sub-lingual calcium antagonists should be discouraged owing to the risky fast action of this administration route. 6. In case of cerebral haemorrhage antihypertensive therapy should be given if blood pressure is >180 mm Hg systolic or >105 mm Hg diastolic. 7. If blood pressure is lowered by antihypertensive agents in the setting of acute stroke, serial neurological examinations should be performed to look for signs of deterioration such as increasing weakness or reduced level of consciousness. 8. In acute stroke patients with systolic blood pressure <185 mm Hg or diastolic blood pressure <105 mm Hg, antihypertensive therapy is usually not indicated. 9. Although there are no data to support a threshold for treatment of hypotension in stroke patients, we recommend treatment for signs of dehydration, blood pressure that is substantially below the expected level for a given patient (consider past history of hypertension, treated or untreated), or both. Therapeutic options should include IV fluids, treatment of congestive heart failure and bradycardia, and consideration of pressor agents such as dopamine.

In acute stroke patients, maintenance of a balanced fluid status is recommended. Intravenous fluid therapy should be administered according to the fluid balance.

Hypotonic solutions (NaCl 0,45% or glucose 5%) are not recommended in acute stroke patients due to the risk of brain oedema.

Glucose solutions are not recommended due to the detrimental effects of hyperglycaemia.

Isotonic saline solutions are recommended for intravenous fluid therapy of acute stroke patients.

Experimental and clinical evidence show that hyperthermia increases infarct size and negatively influences clinical and functional outcomes.

Hypothermia has been shown to be neuroprotective. About 50% of patients with acute stroke present with fever over the initial 48 h of onset.

Treatment of body temperature $\geq 37^{\circ}\text{C}$ is recommended in acute stroke patients, preferably with paracetamol.

In case of fever, the timely search of a possible infection is recommended in order to start as early as possible an appropriate treatment

Prophylactic antibiotic treatment is not recommended in immunocompetent stroke patients.

Urinary tract infection is the most frequent infectious complication in acute stroke. Its risk is associated with the use of indwelling urine catheter. Administration of a semi-synthetic penicillin or a fluoroquinolone is the first-choice empirical therapy; in severe cases an aminoglycoside may be associated or a carbapenem may be used as monotherapy.

Pneumonia, including aspiration pneumonia, is the second most frequent infectious complication in acute stroke. Initial antibiotic therapy is chosen empirically among carbapenems in monotherapy, or broad-spectrum cephalosprines, or a combination of an aminoglycoside plus a broad-spectrum beta-lactam antibiotic covering also the anaerobes. The administration of a glycopeptide should be considered for possible infection due to methicillin-resistant *S. aureus*. Treatment should be continued up to 7-10 days in the infections by methicillin-susceptible or traditional respiratory bacteria; up to 10-14 days in the infections due to methicillin-resistant *S. aureus* or aerobic gram negative bacteria; and as long as 14-21 days in case of severe multilobar pneumonia.

Decubital ulcers are a severe complication of acute stroke, being associated with increased mortality and poor clinical and functional outcomes. The risk of decubital ulcers is higher in patient with obesity, diabetes mellitus, and malnutrition.

Prevention of decubital ulcers is recommended in acute stroke patients. It should be based on frequent turning (every 1-4 h) of immobilised patients, careful hygiene and use of air-filled or fluid-filled mattress systems.

Protein-energy malnutrition is frequent in patients with stroke. In these patients the assessment of nutritional status is important to early recognise and correct malnutrition. Adequate nutrition is advisable to prevent medical complications, to decrease the length of hospital stay and to improve the quality of life.

The assessment of nutritional status and proper nutritional interventions are recommended as part of the diagnostic and therapeutic work-up in patients with acute stroke in the acute as well as in the rehabilitation settings.

It is recommended that expert nutritionists and dietitians participate in the multidisciplinary team of a stroke unit.

The evaluation of nutritional status and nutritional risk is based on the assessment of anthropometric measures, diet intake, possible comorbidities, biochemical parameters and calculation of integrated nutritional indexes.

In patients able to stand up, measurement of body weight and of abdominal circumference, and calculation of body mass index (BMI) is recommended. In patients unable to stand up, measurement of body weight, (by means of appropriate devices), arm circumference and triceps skinfold thickness is recommended.

Laboratory markers to be used as measures of nutritional status are serum albumin level and lymphocyte count.

An integrated nutritional index, such as the Nutritional Risk Screening, is recommended to be calculated on admission and regularly during the hospitalisation. The frequency of measurements should be adapted to the individual risk of nutritional status failure.

Recommendation 11.9 Grade D

Recommendation 11.10 Grade D

Recommendation 11.11 Grade D

Recommendation 11.12 Grade D

Synthesis 11-1

Recommendation 11.13 Grade D

Recommendation 11.14 Grade D

Recommendation 11.15 Grade D

Synthesis 11-2

Synthesis 11-3

Synthesis 11-4

Recommendation 11.16 Grade D

Synthesis 11-5

Recommendation 11.17 a Grade D

Recommendation 11.17 b Grade D

Synthesis 11-6

Recommendation 11.17 c Grade D

Recommendation 11.17 d Grade D

Recommendation 11.17 e Grade D

Synthesis 11–7	Nutritional support in patients with acute stroke is aimed at preventing and treating protein-energy malnutrition as well as electrolytes or micronutrients imbalance.
Synthesis 11–8	Energy requirement is calculated taking into account degree of physical activity and underlying disease. It is expressed as multiple of basal metabolism: values between 1.2 and 1.5 (according to patient mobility) are recommended, up to 2 in case of hypercatabolism. The intake of at least 25 kcal/kg/day is advisable, then the energy intake should be corrected according to the estimated metabolic needs.
Synthesis 11–9	In stroke patients the suggested protein intake per day is approximately 1 g/kg of body weight, up to 1,2~1,5 g/kg in case of hypercatabolism or when decubital ulcers are present. Timing and way of nutrition depend on the patient's clinical conditions.
Recommendation 11.18 Grade D	In patients with acute stroke, the recommended nutritional approaches are the following: <ul style="list-style-type: none"> • <i>non-dysphagic patients without malnutrition</i>: nutrition per os; • <i>non-dysphagic patients with protein-energy malnutrition</i>: nutrition per os with dietetic integrators; • <i>dysphagic patients</i>: progressive modification of the diet according to degree of deglutition disorder or enteral nutrition, integrated if needed.
Recommendation 11.19 a Grade C	In patients with stroke, enteral nutrition is the first choice way of nutrition.
Recommendation 11.19 b Grade D	Parenteral nutrition is recommended only if the enteral approach is not feasible or is contra-indicated, or if an integration to enteral nutrition is needed.
Synthesis 11–10	Enteral nutrition by means of pump-assisted naso-gastric tube is considered more appropriate than parenteral nutrition for short-term nutrition of patients with acute stroke and severe dysphagia. Care should be exerted to avoid possible problems in the application of the naso-gastric tube, especially in the elderly.
Synthesis 11–11	In patients with delayed gastric emptying, aspiration pneumonia may be not prevented by nasogastric feeding, especially in case of severe brain infarct. In this case the risk of aspiration may be reduced by positioning the tube beyond the Treitz angle.
Recommendation 11.20 Grade D	In patients with dysphagia due to stroke, the placement of PEG (percutaneous endoscopic gastrostomy) tube should be considered within 30 days if dysphagia is expected to persist more than 2 months
Synthesis 11–12	Patients with stroke frequently experience dysphagia, which may negatively influence clinical and functional outcomes, length of hospital stay and mortality rate.
Synthesis 11–13	Possible complications secondary to dysphagia are: malnutrition, aspiration pneumonia, dehydration and haemoconcentration with negative effect on cerebral perfusion and renal function.
Recommendation 11.21 Grade D	In patients with acute stroke a systematic surveillance of swallowing is recommended to prevent complications due to dysphagia.
Recommendation 11.22 Grade D	A standard clinical assessment of the risk of dysphagia, (using for example the Bedside Swallowing Assessment) is recommended in patients with acute stroke. If available, more sensitive and specific instrumental techniques can be utilised in selected centres.
Synthesis 11–14	Experimental and clinical data show that hyperglycaemia increases infarct size, morbidity and mortality rate after stroke. Derangement of glucose metabolism in diabetic patients with stroke is a severe complication. Hypoglycaemia has a detrimental effect on ischaemic brain lesion as well.
Recommendation 11.23 Grade D	When serum glucose level is higher than 200 mg/dl, treatment with insulin is recommended.
Recommendation 11.24 Grade D	Immediate correction of hypoglycaemia is recommended in acute stroke patients, by intravenous dextrose bolus, combined with thiamine 100 mg in case of malnutrition or alcohol abuse.
Synthesis 11–15	Stroke is frequently complicated by dysfunctioning micturition related to site and size of brain lesion. Urine incontinence in the early phase of acute stroke is an independent prognostic predictor of death and severe disability after stroke. Urine retention is associated with a high risk of urinary tract infections.
Recommendation 11.25 Grade D	Insertion of indwelling urine catheter is recommended only in patients with severe urinary dysfunction.
Recommendation 11.26 Grade D	In patients without signs/symptoms of urinary dysfunction, regular check of post-micturition residuals is recommended and intermittent catheterisation is advisable if they are present.

Urinary bladder catheterisation is not recommended unless necessary.

Stroke patients who are at risk of deep venous thrombosis (DVT) should be screened according to standardised criteria before being addressed to a targeted diagnostic work up.

When lower limbs DVT is suspected in a stroke patient, a venous Doppler ultrasonography study is recommended.

Venous Doppler ultrasonography is not recommended as routine study in patients with acute stroke.

Systematic measurement of D-dimer for DVT diagnosis is not recommended.

Treatment of factors known to increase intracranial pressure, such as hypoxaemia, hypercarbia, fever and head positioning (elevation of up to 30°), is recommended.

Treatment of brain oedema is recommended only in case of rapid deterioration of consciousness and appearance of other clinical signs of cerebral herniation with or without radiological signs of space-occupying lesion.

Corticosteroids are not recommended as treatment of severe brain oedema due to stroke. Furthermore they are not recommended as systematic treatment of stroke.

Intravenous administration of furosemide (40 mg)

- **is recommended** as an emergency treatment of rapid clinical deterioration in stroke complicated by severe brain oedema,
- **is not recommended** for long-term therapy.

Osmotherapy with glycerol or mannitol is recommended for more prolonged (few days) treatment of severe brain oedema.

Short-acting barbiturates are not recommended for long-term therapy of brain oedema due to stroke.

In large infarct lesions expanding due to oedema, if response to pharmacological therapy is poor, surgical decompression (hemicraniectomy) can be considered, especially in young patients with involvement of the non-dominant hemisphere and without relevant comorbidity. .

EEG examination has poor diagnostic and prognostic value in relation to the stroke event itself. It is useful for differential diagnosis in the clinical suspect of an epileptic event mimicking stroke

Antiepileptic therapy is not recommended as prophylactic in patients with recent stroke who have no seizures.

Administration of antiepileptic drugs in patients with acute stroke:

- **is not recommended** after a first seizure
- **is recommended** in recurrent seizures, avoiding the use of phenobarbital for its detrimental effect on functional recovery.

The standard anticonvulsant therapy of status epilepticus is the recommended treatment also for status epilepticus after stroke, carefully monitoring for possible detrimental side effects on stroke.

In patients with acute stroke, an early rehabilitative approach is recommended.

In stroke patients, limb mobilisation is recommended at least 3-4 times a day.

Encouraging and motivating patients with stroke to participate to daily activities is recommended.

Selection of drugs with no detrimental effect on functional recovery is recommended.

Promotion of early standing position, after trying sitting position within the third day, is recommended, if not contra-indicated.

Promotion of the participation of patient and relatives to care and rehabilitation processes is recommended.

Recommendation 11.27 Grade D

Synthesis 11–16

Recommendation 11.28 a Grade D

Recommendation 11.28 b Grade D

Recommendation 11.29 Grade D

Recommendation 11.30 Grade D

Recommendation 11.31 Grade D

Synthesis 11–17

Recommendation 11.32 a Grade D

Recommendation 11.32 b Grade D

Recommendation 11.32 c Grade D

Synthesis 11–18

Synthesis 11–19

Recommendation 11.33 Grade D

Recommendation 11.34 Grade D

Recommendation 11.35 Grade D

Recommendation 11.36 Grade A

Recommendation 11.37 Grade D

Recommendation 11.38 Grade D

Recommendation 11.39 Grade D

Recommendation 11.40 Grade D

Recommendation 11.41 Grade D

		SECONDARY PREVENTION: LONG TERM PHARMACOLOGICAL THERAPY
Recommendation 12.1	Grade A	Aspirin (100-325 mg per day) is the recommended treatment in TIA and non cardio-embolic ischaemic stroke.
	*GPP	The SPREAD group recommends the dose of 100 mg per day for long-term therapy.
Recommendation 12.2	Grade A	Clopidogrel (75 mg per day) and the combination aspirin (50 mg per day) plus dipyridamole (400 mg per day) are recommended as a safe and effective alternative to aspirin. Ticlopidine (250 b.i.d.) is effective as well but it shows a less favourable tolerability profile.
Recommendation 12.3	Grade A	In patients with stroke or TIA, if aspirin is poorly tolerated or ineffective, treatment with clopidogrel (75 mg per day) or ticlopidine (250 b.i.d, with blood count assessed twice monthly for the first 3 months) is recommended .
Recommendation 12.4	Grade C	In patients with cardio-embolic stroke or TIA associated with heart or valvular diseases with embolic potential, oral anticoagulation (target INR between 2.0 and 3.0) is recommended .
Synthesis 12-1		In selected and appropriately trained patients, self-monitoring of oral anticoagulation is feasible provided that regular checks are performed by the general physician.
Recommendation 12.5	Grade D	After stroke or TIA, lowering of high blood pressure is recommended , preferably using agents active on the renin-angiotensin system.
Synthesis 12-2		The PROGRESS Study showed that the ACE inhibitor perindopril alone or, with greater benefit, in combination with indapamide reduces the risk of recurrent stroke.
Recommendation 12.6	Grade B	In patients with stroke or TIA and elevated cholesterol levels, cholesterol-lowering therapy is recommended independently of previous coronary events.* * The strength of evidence is mostly based on the results of HPS study on administration of simvastatin (40 mg per day).
Synthesis 12-3		The HPS study showed the efficacy of simvastatin in reducing the risk of recurrent vascular events, even in patients with normal cholesterol levels.
Recommendation 12.7	Grade A	After a non cardio-embolic stroke or TIA, oral anticoagulation is not recommended because there is no documented evidence of an higher benefit compared with antiplatelet therapy at an INR range of 2.0-3.0, while the risk of cerebral haemorrhagic complications is higher at an INR range of 3.0-4.5.
Recommendation 12.8	Grade A	Oral anticoagulation (INR 2.0-3.0) is recommended after a cardio-embolic stroke or TIA associated with non valvular atrial fibrillation.
Recommendation 12.9	Grade A	Aspirin (325 mg per day) is recommended after a cardio-embolic stroke or TIA associated with non valvular atrial fibrillation, when oral anticoagulation cannot be administered.
Recommendation 12.10	Grade B	Indobufen (100-200 mg twice daily) is recommended after a cardio-embolic stroke or TIA associated with non valvular atrial fibrillation, when oral anticoagulation cannot be administered.
Recommendation 12.11	Grade C	Oral anticoagulation (INR 2.0-3.0) is recommended after a cardio-embolic stroke or TIA associated with isolated dilated cardiomyopathy.
Recommendation 12.12a	Grade C	Aspirin is recommended after a thrombo-embolic stroke or TIA associated with patent foramen ovale, if no deep venous thrombosis is documented and this is the first thromboembolic event.
Recommendation 12.12b	Grade C	Oral anticoagulation (INR 2.0-3.0) is recommended after stroke or TIA associated with patent foramen ovale combined with atrial septal aneurysm or with coagulation abnormalities, if other possible causes are excluded.
Recommendation 12.12c	Grade C	After a recurrent stroke or TIA associated with patent foramen ovale, in patients <45 years, with atrial septal aneurysm and a wide right-to-left shunt, who are already on adequate oral anticoagulation or if anticoagulation is contra-indicated, percutaneous transcatheter closure of the foramen is recommended .
Recommendation 12.13	Grade C	After a recurrent stroke or TIA in patients with prosthetic heart valve who are already on adequate oral anticoagulation, the combination of oral anticoagulants plus dipyridamole (400 mg per day) or aspirin (100 mg per day) is recommended .

SURGICAL TREATMENT

The benefit from carotid endarterectomy is minor in symptomatic patients with 50-69% stenosis (NNT=22 to prevent ipsilateral stroke, non significant NNT to prevent disabling stroke and death) and noticeable for 70-99% stenosis (NNT=6 and 14 respectively), provided that there is no near-occlusions. The benefit from endarterectomy is marginal in patients with carotid near-occlusion. The benefit of endarterectomy is still greater in patients with a high risk score according to the current models (NNT=3) and little if any in patients with low risk score (NNT=100).

Carotid endarterectomy is recommended for patients with symptomatic (<6 months) stenosis greater than 70% (NASCET criteria).

Carotid endarterectomy is not recommended for patients with symptomatic stenosis less than 50% (NASCET criteria).

Carotid endarterectomy is recommended for patients with symptomatic stenosis of 50-69% (NASCET criteria), even though the benefit is minor at least during the first years of follow-up while increasing in the subsequent years.

Carotid endarterectomy is recommended as definitely beneficial for patients with symptomatic stenosis of 50-69% (NASCET criteria) only among those with high risk score in validated models (recent hemispheric and not ocular symptoms, complicated plaques, elderly patients, males, non diabetics).

The benefit from carotid endarterectomy is not yet conclusively determined in asymptomatic patients. Important ongoing trials should identify the subsets of patients at risk of ipsilateral stroke and expected to have a greater benefit from carotid surgery.

Carotid endarterectomy is recommended for patients with asymptomatic stenosis greater than 60% (NASCET criteria) **only** in centres with perioperative complication rate of less than 3%. However, the benefit, expressed as absolute risk reduction, is small.

In patients who are candidates to carotid endarterectomy, coronary angiography **is recommended** when there is clinical or non-invasive instrumental evidence of severe coronary artery disease.

In patients who are candidates to carotid endarterectomy and have an associated severe coronary artery disease, it **is recommended** to consider a possible coronary revascularization procedure, carrying out the two interventions either separately (treating first the symptomatic district), or in combination.

The timing of carotid endarterectomy should in symptomatic patients be as follows:

- carotid surgery **is recommended** as early as possible for patients with TIA or minor stroke and normal CT scanning;
- early carotid endarterectomy **is recommended** for patients with stable neurological conditions and minimal CT lesions;
- early carotid endarterectomy **is not recommended** for patients with large infarction on CT scanning, independently of the severity of neurological deficits.

Carotid Doppler ultrasonography is recommended as a first-choice investigation for the etiological work up of stroke and for screening possible candidates to carotid endarterectomy.

Conventional angiography of cerebral vessels was the gold standard examination in trials on carotid endarterectomy, therefore carotid Doppler ultrasonography **is recommended** for preoperative measurement of carotid stenosis only after verifying its accuracy.

Supra-aortic vessel MRA and/or CTA **are recommended** if Doppler US examination does not result reliable in the individual patient.*

The SPREAD panel **recommends** conventional angiography **only** when Doppler ultrasonography and MR/CT angiography yield discordant results or if they are not feasible.

Intra-operative monitoring of cerebral functions by means of reliable techniques (EEG, Somatosensory Evoked Potentials, Transcranial Doppler) **is recommended** during general anaesthesia.

Loco-regional anaesthesia **is recommended** because it allows a more reliable monitoring of cerebral functions and it is associated with a lower perioperative risk of death, stroke, myocardial infarction and respiratory complications, compared with general anaesthesia.

Temporary selective shunting **is recommended** for cerebral protection during both general and loco-regional anaesthesia.

Synthesis 13-1

Recommendation 13.1 **Grade A**

Recommendation 13.2 **Grade A**

Recommendation 13.3 a **Grade A**

Recommendation 13.3 b **Grade B**

Synthesis 13-2

Recommendation 13.4 **Grade A**

Recommendation 13.5a **Grade D**

Recommendation 13.5b **Grade D**

Recommendation 13.6 **Grade C**

Recommendation 13.7 a **Grade C**

Recommendation 13.7 b **Grade C**

Recommendation 13.7 c **Grade D**

*GPP

Recommendation 13.8 a **Grade D**

Recommendation 13.8 b **Grade D**

Recommendation 13.9 **Grade D**

Synthesis 13–3	In spite of a trend, in non-randomised studies, in favour of carotid patching in lowering the incidence of perioperative stroke and death, acute postoperative internal carotid artery thrombosis and recurrent stenosis, no conclusive data are available yet. Further evidence is needed from randomised studies comparing primary closure with systematic patching and, mostly, with selective patching.
Recommendation 13.10 a Grade A	The change of current general practice of endarterectomy for carotid stenosis in favour of endovascular procedures is not recommended , given the lack of conclusive evidence on superiority of angioplasty/stenting compared with endarterectomy.
Recommendation 13.10 b Grade C	Angioplasty/stenting is recommended only in selected cases such as carotid re-stenosis following endarterectomy, intracranial carotid stenosis and post-radiation stenosis. It is not recommended in case of intraluminal thrombosis or severe calcification of supra-aortic vessels.
*GPP	The SPREAD panel recommends the endovascular procedures in case of severe vascular or cardiac comorbidities.
Recommendation 13.11 Grade A	Both conventional and eversion carotid endarterectomy may be recommended for patients with carotid stenosis, provided that they are performed in centres with a perioperative complication rate (all strokes and death) of less than 3%.
Recommendation 13.12 Grade B	Centres performing carotid endarterectomy are recommended to assess and make known their own perioperative complication rate (all strokes and death), since this could have an impact on decision about carotid surgery especially in patients with asymptomatic carotid stenosis.
Recommendation 13.13 Grade D	During carotid endarterectomy, the intraoperative assessment of defects is recommended for possible repair and quality control. The intraoperative control is associated to a significant reduction of post-operative complications such as re-stenosis and long-term recurrence of stroke.
Recommendation 13.14 Grade A	The antiplatelet therapy is recommended before, during and after surgery, unless it is contra-indicated.
Recommendation 13.15 Grade C	Carotid surgery of severe, symptomatic re-stenosis is recommended .
Recommendation 13.16 Grade D	Intensive monitoring of possible re-stenosis is not recommended . US control is recommended at 3 and 9 months after surgery and every year thereafter.

REHABILITATION AND CONTINUED CARE

After the acute phase of stroke, structured care of disabled patients is recommended, programming the interventions in dedicated, multidisciplinary services taking into account the long-term needs of the patient.

Care activities for rehabilitation of patients with stroke are different according to the timing of intervention, and the involvement of different professional figures depends on proposed goals, patient's clinical conditions and available resources.

The selection of post-acute patients to be addressed to rehabilitation services is based upon benefit likelihood and resource availability.

It is recommended to establish an efficient organisation dedicated to stroke patient care through an expert, multidisciplinary teamwork.

According to the available resources, the team should comprise non-medical (nurses, physiotherapists, speech therapists, occupational therapists, neuropsychologists, social workers) as well as medical (physicians specialised in cerebrovascular disease management, general physicians) professionals, with the involvement of patient organisation representatives.

The identification of predictors of functional recovery is recommended, to adequately programme the care interventions and allocate the available resources.

Elderly age does not limit the functional recovery after stroke, unless it is associated with negative outcome predictors.

A higher risk for institutionalisation is reported in female subjects compared with married males, but a clear causal relationship between these factors has not been found.

Patients who were institutionalised at stroke onset are at high risk of further deterioration of their functional independence.

Non disabling comorbidities of stroke patients can negatively influence mortality rate, but they do not reduce the level of functional recovery despite a possible delay.

Total anterior cerebral infarctions, defined according to Bamford classification, independently of the side, are associated with higher residual disability. There are no significant differences of functional outcome for the other Bamford's subtypes.

It is recommended to plan the rehabilitation treatment according to predictors of dependency, such as stroke severity at onset (coma, incontinence, severe neurological impairment) or other specific clinical features (severe muscle tone disturbances, dysphagia, hemineglect, global aphasia).

Coma at stroke onset, persisting urinary and bowel incontinence and persistent paralysis are negative predictors of independence.

Persistent flaccidity or severe spasticity negatively influence motor recovery.

Severe aphasia negatively affects recovery of independence in activity of daily living.

Spatial hemineglect negatively affects motor recovery.

A moderate disability and recovery of trunk control are associated with a higher effectiveness of the rehabilitation treatment.

Functional assessment by means of validated scales is recommended in planning the rehabilitation treatment of stroke patients.

An early screening for mood disturbances is recommended as part of the rehabilitation assessment of stroke patients. The diagnosis of depression should be made according to a multidimensional approach and by means of standardised scales for evaluating and monitoring symptoms.

Given the facilities provided by the Italian National Health Service, the socio-economic level of stroke patients should not play a predictive role on recovery. Familiar and social networks favour returning home from hospital and support long term care. Length of hospital stay may be reduced by active involvement of caregivers in rehabilitation planning and by an efficient healthcare and social local support.

Referral of stroke patients to dedicated multidisciplinary Stroke Units is associated with a better functional outcome.

All the specific interventions targeted to recovery of impairments are recommended for planning the rehabilitation treatment in individual patients. The rehabilitation programme has to be regularly updated according to the course of recovery.

Recommendation 14.1 Grade D

Synthesis 14-1

Synthesis 14-2

Recommendation 14.2 *GPP

Recommendation 14.3 Grade D

Synthesis 14-3

Synthesis 14-4

Synthesis 14-5

Synthesis 14-6

Synthesis 14-7

Recommendation 14.4 Grade D

Synthesis 14-8

Synthesis 14-9

Synthesis 14-10

Synthesis 14-11

Synthesis 14-12

Recommendation 14.5 Grade D

Recommendation 14.6 Grade D

Synthesis 14-13

Synthesis 14-14

Recommendation 14.7 Grade D

Recommendation 14.8	Grade D	Pre- and post-rehabilitation assessment of disability is recommended by means of valid and widely used scales such as the Barthel Index and the Functional Independence Measure (FIM).
Recommendation 14.9	Grade D	Assessment of clinical, functional and socio-economic status of a patient with stroke is recommended soon after the admission in a rehabilitation unit. Both disability and impairment (motor and/or cognitive) should be measured.
Recommendation 14.10	Grade D	A comprehensive cognitive and mood assessment is recommended in patients with communication, cognitive and emotional disturbances.
Recommendation 14.11	Grade D	Identification of rehabilitation goals according to an outcome-related temporal profile is recommended . Patients should be kept informed of the medium and long term goals of rehabilitation and of the presumed course of recovery.
Recommendation 14.12	*GPP	In planning the rehabilitative programme, the identification of goal priority is recommended according to the functional hierarchy of recovery and to the care needs.
Recommendation 14.13	Grade C	The active involvement of patients and carers together with the multidisciplinary team, co-ordinated by a stroke rehabilitation expert, is recommended in the rehabilitation process. The team should regularly conduct meetings to identify the patient's problems, set the rehabilitation goals, monitor the progress and plan the discharge.
Recommendation 14.14	*GPP	The assessment of the available resources is recommended before planning the rehabilitation programme, to ensure the long term feasibility of interventions.
Recommendation 14.15	Grade D	Evaluation of possible use of orthoses and aids is recommended when planning a rehabilitation programme based on compensatory strategies.
Recommendation 14.16	Grade D	Regular follow ups are recommended to verify the achievement of the set goals and to assess the functional independence by means of standardised scales (Barthel Index and Functional Independence Measure).
Recommendation 14.17	*GPP	Rehabilitative services are recommended to adopt a system of quality assessment, preferably ISO (International Organization for Standardization) certification, to improve quality, efficiency and appropriateness of rehabilitative interventions.
Recommendation 14.18	Grade D	Involvement of patients and carers in the definition of the rehabilitation programme is recommended to improve the quality of care. Caregiver training and social support interventions should be planned.
Recommendation 14.19	Grade D	The stroke team professionals are recommended , while planning the discharge after the acute phase of stroke, to inform the rehabilitation hospital or the territorial services that will receive the patients, about the functional prognosis and to supply all the documentation useful for transfer of care.
Synthesis 14–15		Pharmacological interventions possibly helping in recovery after stroke are under investigation. Possible detrimental effects on recovery of drug treatments should also be taken into account.
Recommendation 14.20	Grade A	Professionals working in services (hospital or territorial) dedicated to stroke care should be expert in both cerebrovascular diseases and rehabilitation. They should be trained in the use of standardised treatment protocols and continuing education programmes for health professionals, patients and caregivers.
Recommendation 14.21	*GPP	The specific age-related care needs are recommended to be considered by the services involved in the management of patients with stroke.
Recommendation 14.22	Grade D	Assessment of progress against the agreed short- and long-term rehabilitative goals is recommended , in relation to the activity of the whole team and of the single professionals.
Synthesis 14–16		Immobility and functional deficits in the acute phase of stroke may be the cause of a number of physical and functional impairments that negatively interfere with recovery.
Recommendation 14.23	Grade C	It is recommended that the early rehabilitation programmes consider state of consciousness, cognitive problems, swallowing impairment, nutritional status, risk of pressure sores and mobility.
Recommendation 14.24	Grade A	The involvement of the rehabilitative staff is recommended within the first week of hospitalisation.
Recommendation 14.25	Grade C	The rehabilitation treatment of stroke patients is recommended to be intensive, compatibly with patient's conditions and service characteristics, and aimed at promoting ability to carry out practically applicable activities.
Synthesis 14–17		The functional recovery of stroke patients is based upon motor recovery and compensatory strategies. The available evidence is not sufficient to consider any one approach to treatment more efficacious than others in promoting effective rehabilitation. Controlled trial are needed to investigate the effectiveness of each single approach.

It is recommended that carers are kept fully informed on the problems associated with stroke, especially cognitive and behavioural problems and urinary incontinence. They should also be given information on the services provided by local and national agencies.

The involvement of social workers **is recommended** to organise and support the appropriate care resources, thus reducing the family distress.

Reassessment of patients with residual disability lasting longer than 6 months after stroke **is recommended** to set further rehabilitation goals.

Careful evaluation of patients with severe stroke **is recommended** to identify potential recovery and plan the most efficacious care pathway.

Therapeutic positioning and segmental limb mobilisation **are recommended** to prevent contractures, respiratory infections, shoulder pain and pressure sores.

Encouraging patients to participate in daily activities and to leave the bed early (possibly within the third day) is recommended.

Early rehabilitation treatment promotes the recovery of postural control and gait. No specific approach was proven to be better than any other. Some evidence suggests a benefit of the task-specific training.

A rehabilitation programme for the plegic upper limb within the first 3 months is recommended.

Functional recovery of upper limb is a short- and medium-term goal of the rehabilitation of stroke patients. An integrated behavioural-physical approach is suggested as beneficial to recovery, but evidence is insufficient to conclude that any one approach is more effective than another. Selected patients may benefit from constraint-induced movement therapy.

Speech and language therapy is aimed at:

- a. recovering general communication, verbal communication, reading, writing and calculation;
- b. enhancing compensatory strategies for communication functions;
- c. instructing carers on methods for maximising communication.

Most common treatments for aphasia are:

- a. impairment-based approaches;
- b. recovery of communication functions according to neurocognitive models of language;
- c. stimulus-response approaches.

Involvement of speech therapists and a careful evaluation are recommended for patients with communication disturbances following stroke.

Speech and language interventions should be adequately tailored to the individual patient's communication disturbances and defined according to the therapist's expertise.

In patients with selective communication disturbances, a targeted specific rehabilitation treatment is recommended.

Visuospatial and attention disturbances are associated with a poorer functional outcome of stroke patients.

Therapy of unilateral visuospatial neglect is aimed at improving exploration of personal and peripersonal space.

Treatments of hemineglect are based on specific strategy training and on approaches directed to improve general attention.

Specific strategy training is recommended to treat visuospatial attention disturbances. Further evidence on effectiveness of prism adaptation and vestibular stimulation approaches is needed.

Treatment of apraxia is aimed at restoring the ability of gesture-programming with stimulus-response exercises or gesture reintegration, according to classical cognitive models, or ecologic approaches.

Specific treatment of oral or limb apraxia is recommended in patients with apraxic disorders persisting after the acute phase of stroke.

Evidence from two Cochrane reviews does not consent to support or reject the effectiveness of cognitive rehabilitation for attention deficits or for memory problems following stroke.

Patient's compliance and motivation, appropriate carer training and efficient cooperation between all members of the rehabilitative team are recommended to carry out programmes for neuropsychologic assessment and rehabilitation.

Recommendation 14.26 Grade C

Recommendation 14.27 Grade C

Recommendation 14.28 Grade C

Recommendation 14.29 Grade C

Recommendation 14.30 Grade B

Recommendation 14.31 Grade B

Synthesis 14-18

Recommendation 14.32 Grade C

Synthesis 14-19

Synthesis 14-20

Recommendation 14.33 Grade D

Recommendation 14.34 Grade B

Recommendation 14.35 Grade C

Synthesis 14-21

Recommendation 14.36 Grade A

Synthesis 14-22

Recommendation 14.37 Grade C

Synthesis 14-23

Recommendation 14.38 *GPP

Synthesis 14–24		The use of sensory-motor integration methods, acupuncture and transcutaneous electrical nerve stimulation (TENS) is supported more by experimental data than by clinical evidence. There are no additional benefits from the combination of functional electrical stimulation (FES) or TENS plus acupuncture or other physiotherapy approaches. These techniques may be used in selected cases for the treatment of painful syndromes.
Recommendation 14.39	*GPP	Acupuncture or transcutaneous electrical nerve stimulation (TENS), alone or in combination with physiotherapy, for the treatment of painful syndromes other than shoulder pain, are recommended only within controlled clinical trial.
Recommendation 14.40	Grade C	Transcutaneous electrical nerve stimulation (TENS) is recommended for the treatment of hemiplegic painful shoulder only in selected cases.
Recommendation 14.41	Grade C	The assessment of factors that may be responsible for upper limb pain is recommended in both the acute and post-acute phase.
Synthesis 14–25		There is insufficient evidence supporting the role of physiotherapy in the treatment of shoulder pain following stroke. Electrical stimulation increases articular range of motion without obtaining a persisting improvement of focal disability.
Recommendation 14.42 a	Grade B	It is recommended that the risk of aspiration is timely screened by trained personnel within the first few days after stroke. In case of swallowing disturbances, speech and language therapists should be involved and appropriate interventions should be programmed.
Recommendation 14.42 b	Grade D	Prevention of malnutrition due to dysphagia is recommended by enteral nutrition approaches, such as naso-gastric tube and percutaneous endoscopic gastrostomy.
Recommendation 14.42 c	Grade D	Weaning from enteral nutrition should be considered in patients with positive prognostic factors and it should be performed by specialised personnel, following a standardised approach based on clinical, videofluoroscopic and/or endoscopic monitoring
Recommendation 14.42 d	Grade D	During all phases of weaning from enteral feeding, an appropriate energy and water intake is recommended.
Recommendation 14.43	*GPP	Units dedicated to stroke care should implement protocols for the management of urinary and faecal incontinence or retention. Assessment of patients with incontinence is a nursing practice that should be started at time of admission together with all the specific care activities. The protocols should provide indications about the use of urinary catheter or the need of urodynamic or anorectal function assessment, and on the most adequate continence aids to be selected during hospital stay and after discharge, considering also possible limitation of sexual activity.
Recommendation 14.44	Grade C	In patients with urinary incontinence, a specialised, clinical and functional assessment, including an urodynamic assessment, is recommended to plan re-education to voluntary micturition.
Recommendation 14.45	Grade D	All patients who have problems with activities of daily living following stroke should have access to an occupational therapist with specific knowledge and expertise in neurological care.
Recommendation 14.46	Grade D	Regular assessment and advice on appropriate equipments and adaptations is recommended. Aids should be selected according to patient and carer expectations and should be provided timely.
Recommendation 14.47	*GPP	It is recommended that appropriate environment adaptations are set up before patients return home from hospital.
Recommendation 14.48	*GPP	It is recommended that, at the time of discharge from the hospital, all territorial resources and outpatient facilities be activated to promote a successful social reintegration of the patient, according to the indications provided by the stroke care team after the acute phase.
Recommendation 14.49	Grade B	Encouraging stroke survivors to return to work is recommended if allowed by their functional status. Whenever necessary, counselling regarding actual job options should be offered to patients.
Synthesis 14–26		Beside impairments following stroke, patients may be also affected by previous comorbidities and by stroke complications (spasticity, depression, malnutrition, articular painful syndromes, falls...). All these ailments should carefully be assessed and treated because they negatively affect the rehabilitative processes.
Recommendation 14.50	Grade D	Antispastic therapy is recommended if spasticity is associated with pain or if it endangers the functional recovery.

Injection of Botulinum Toxin **is recommended** as a strategy for the treatment of focal spasticity, usually of upper or lower limbs, in patients who exhibit poor response or tolerability to oral antispasmodic drugs (e.g. tizanidine).

Among stroke survivors who are able to walk, it **is recommended** to:

1. identify patients at risk of falling,
2. perform specific rehabilitative interventions,
3. apply all the environmental adaptations useful to reduce the risk of falls, such as improved bath access, stronger lighting, adjustment of slippery floors and increased surveillance.

There is not sufficient evidence yet to support or refute the benefits of cognitive rehabilitation for patients with problems of attention or memory, nevertheless, considering the negative functional impact of cognitive impairment on stroke patients, approaches directed at exploiting the residual abilities and at providing appropriate caregiver education **are recommended**.

Early after stroke, appropriate shoulder positioning, using soft supports and avoiding traction manoeuvres on plegic shoulder **is recommended**.

After the acute phase of stroke, radiology examination of shoulder **is recommended** if a subluxation occurs.

Shoulder slings and functional electrical stimulation (FES) **are recommended** for shoulder subluxation.

Local injection of corticosteroids **may be recommended** for severe shoulder pain.

Analgesic treatment of persistent central pain **is recommended** by using antiepileptic drugs (gabapentin, etc.) or tricyclic antidepressants (amitriptyline, etc), to be individually titrated.

Assessments of nutritional status should be recorded in the patients' clinical documents that are transferred within the different phases of hospital stay, because nutritional needs may change along the time. Data from nutritional documents should be studied as possible prognostic indicators.

Evaluation of pulse oxymetry and polysomnography **is recommended** to diagnose a sleep apnoea syndrome in patients with stroke who are obese or affected by heart diseases. Interventions for weight reduction, alcohol cessation, nasal cavity widening are recommended as well as avoiding sleeping in supine position.

Rehabilitative options may be provided within the context of a network of dedicated services that are differentiated into intensive or extensive rehabilitation according to type and intensity of interventions.

Intensive rehabilitation should be performed within the context of a tailored network of both inpatient and outpatient dedicated services.

Referral to territorial rehabilitative services **is recommended** for patients with minor stroke.

Factors such as elderly age and neurological severity of stroke should not be considered as exclusion criteria for accessing hospital rehabilitation.

In patients with slight-to-moderate disability following stroke, early discharge from the rehabilitation hospital **is recommended** if territorial services are able to provide a teamwork as dedicated and expert as that acting in the hospital.

Hospital units dedicated to stroke care **are recommended** to adopt discharge protocols and local guidelines and to issue timely advice to the territorial inpatient or outpatient rehabilitation services.

Before hospital discharge of a stroke survivor, planning territorial transfer of care **is recommended** by involving the patient, the caregivers and the family physician and by activating social and healthcare local services.

Planning a day-hospital rehabilitation approach **is recommended** for those patients who need continuation of intensive, multidisciplinary (physiotherapy, cognitive and occupational) rehabilitation after hospital discharge.

Planning ambulatory rehabilitation **is recommended** for those patients who need an interdisciplinary, rehabilitative care but not an intensive approach.

Home rehabilitation **is recommended** when patients and caregivers need a specific training in performing exercises and mobilisation, in using aids and prostheses or in practicing occupational therapy activities.

Recommendation 14.51 **Grade B**

Recommendation 14.52 **Grade D**

Recommendation 14.53 ***GPP**

Recommendation 14.54 a ***GPP**

Recommendation 14.54 b ***GPP**

Recommendation 14.54 c **Grade D**

Recommendation 14.54 d **Grade D**

Recommendation 14.55 **Grade C**

Recommendation 14.56 ***GPP**

Recommendation 14.57 **Grade D**

Synthesis 14–27

Recommendation 14.58 **Grade C**

Recommendation 14.59 **Grade C**

Recommendation 14.60 **Grade B**

Recommendation 14.61 **Grade B**

Recommendation 14.62 ***GPP**

Recommendation 14.63 ***GPP**

Recommendation 14.64 **Grade D**

Recommendation 14.65 **Grade D**

Recommendation 14.66 **Grade D**

Recommendation 14.67	Grade D	Caregivers should be provided with all the aids useful to help stroke patients and to safely perform positioning and transfer.
Recommendation 14.68	Grade D	Before hospital discharge of stroke patients, assessment of home is recommended to set up all the appropriate adaptations.
Recommendation 14.69	Grade B	A multidisciplinary team should review the long-term rehabilitation needs of stroke survivors living at home within one year after stroke onset.
Synthesis 14–28		Stroke is a frequent cause of death and disability in the elderly. In elderly patients, disability following stroke often superposes to that due to comorbidities.
Recommendation 14.70	Grade D	The territorial stroke care team should regularly (every 6 months) assess ability and participation of elderly stroke patients to daily activities.
Recommendation 14.71	Grade D	Stroke survivors should undergo regular cardiovascular and metabolic assessments, as well as monitoring of body weight, to control cerebrovascular risk factors and to adjust the pharmacological therapy according to clinical and laboratory changes.
Recommendation 14.72	Grade D	Long-term rehabilitation of stroke survivors is recommended in case of deterioration of functional status and it should be aimed at achieving specific rehabilitative goals.
Recommendation 14.73	*GPP	A long-term rehabilitation programme promoting independence in daily activities is recommended to reduce the deterioration of the independence status obtained by the intensive or extensive rehabilitation.
Recommendation 14.74	*GPP	Assessment and treatment of comorbidities are recommended during rehabilitation of elderly patients.
Recommendation 14.75	Grade B	A multidimensional geriatric assessment is recommended in planning the rehabilitative interventions for elderly patients.
Recommendation 14.76	Grade D	Services for elderly patients should be organised as a network directed by the Geriatric Evaluation Unit and coordinated by a case manager who assesses the care needs and addresses the patients to the best fitting service.
Synthesis 14–29		Oldest patients are often excluded from rehabilitation for no valid reasons. This approach considerably limits their possible recovery and the preservation of their functional independence.
Recommendation 14.77	*GPP	Rehabilitative protocols for elderly patients are recommended to be flexible and to have a longer duration than in younger patients, if necessary.
Synthesis 14–30		In the rehabilitative phase of stroke patients, nutritional strategies are aimed at preventing and treating malnutrition. Planning of nutritional treatment is based on the assessment of swallowing function, on the use of diagnostic protocols to evaluate nutritional status and nutritional risk and on the implementation of procedures for appropriate nutritional management during hospital stay. Nutritional needs should be gradually met, especially after prolonged fasting or in case of nutritional disturbances.
Recommendation 14.78 a	Grade D	It is recommended that non-dysphagic patients with normal nutritional status are fed with normal oral diet tailored to the age- and sex-related nutritional needs according to Italian Recommended Nutrients Levels (LARN). Disease-specific diets have to be applied in case of comorbidities.
Synthesis 14–31		The dietary treatment of dysphagia consists of modification of food and liquid density according to four different levels of bolus consistency: mashed food, chopped food, soft food and modified normal food. Nutritional supplementation is recommended if dietary intake is insufficient.
Recommendation 14.78 b	Grade D	In patients with protein-energy malnutrition, it is recommended to increase the dietary intake to obtain a gradual correction of the nutritional deficiencies, also through nutritional supplementation or enriched food, if necessary.
Recommendation 14.78 c	Grade D	In patients with protein-energy malnutrition and a proven insufficient dietetic intake, enteral nutrition by means of naso-gastric tube or percutaneous endoscopic gastrostomy (PEG) tube is recommended .
Recommendation 14.79	Grade C	In dysphagic patients who can have an adequate oral nutritional intake, a progressively modified diet is recommended according to four different levels of bolus consistency: mashed food, chopped food, soft food and modified normal food. In cases of severe dysphagia, artificial nutrition is recommended.
Synthesis 14–32		At the time of discharge, the members of the rehabilitative team provide the patient and the carers with a dietetic programme designed according to the patient's needs and the practical information that favours reaching the energy, fluid and nutritional requirements. The carers should be informed and trained on how to monitor the nutritional status at home, by checking the body weight and the food intake.

Advice and education on stroke and on the most appropriate behaviour may be useful in any phase of the disease, if given in a proper way. Further studies are needed to investigate what kind of information and which modality of diffusion are the most appropriate to implement. Patients and caregivers should be involved in designing such studies.

Education and advice of patients and carers have a relevant role for stroke awareness. Such interventions are recommended to be performed through regular meetings between patients, caregivers and members of the interdisciplinary team.

From the acute phase of stroke up to social reintegration, appropriate places and scheduled times are recommended to be set for promoting meeting, talking and collaboration with the patient.

Interventions, targeted to promote education and participation of caregivers and patients to the care activities, are recommended because they can improve psychological well-being of stroke patients and help rehabilitation.

Implementation of a dedicated phone line answered by expert personnel is recommended for stroke survivors and their carers to plan interventions and to provide counselling whenever necessary.

Synthesis 14–33

Recommendation 14.80 Grade A

Recommendation 14.81 Grade D

Recommendation 14.82 Grade D

Recommendation 14.83 Grade D

POST-STROKE COGNITIVE IMPAIRMENT AND MOOD DISORDERS	
Synthesis 15-1	The onset of a depressive episode is frequent within 6-12 months of stroke. About 30% of stroke victims is reported to have mood disorders, even if there is a wide variability between studies due to diagnostic and methodological differences.
Synthesis 15-2	The presence of a possible post-stroke depression should be carefully investigated since confounding somatic symptoms and variability of diagnostic approaches may lead to an under- or overestimation.
Synthesis 15-3	Aphasia, anosognosia, hemineglect and cognitive impairment, may affect the diagnosis of post-stroke depression.
Recommendation 15.1	Grade C
Synthesis 15-4	A multidimensional clinical approach (conversation with patients, relatives, non-professional health workers and use of specific tests and scales), in combination with the DSM-IV-TR criteria, is recommended for the diagnosis of post-stroke depression.
Recommendation 15.2	Grade C
Synthesis 15-5	The scales commonly used for psychiatric diagnosis of depression appear to be equally reliable in detecting post-stroke depression, even if the use of lower cut-off values is suggested.
Recommendation 15.3	Grade D
Recommendation 15.4	Grade D
Synthesis 15-6	The use of psychiatric scales is recommended for quantification and monitoring of post-stroke depression.
Synthesis 15-7	At present the Post-Stroke Depression Rating Scale (PSDRS) is the only scale specifically designed to assess post-stroke depression.
Synthesis 15-8	The assessment of post-stroke depression is recommended also in aphasic patients by means of the clinical evaluation and non-verbal tests.
Synthesis 15-9	Searching for a possible post-stroke depression is recommended early in the post-acute phase, before starting rehabilitation and anyway during the first year after stroke to reduce patient's disability, caregiver's burden and costs.
Synthesis 15-10	Patients with post-stroke depression exhibit less melancholy but more somatic complaints (fatigue, sleep and concentration disorders, reduced appetite, etc.) than patients with functional depression. Patients with stroke and depression report more somatic symptoms than stroke patients without depression.
Synthesis 15-11	The distinction between major and minor depression is not widely accepted when applied to post-stroke depression.
Synthesis 15-12	Post-stroke depression has probably a multifactorial aetiopathogenesis. Previous psychiatric and/or cerebrovascular disorders, higher education, severe disability, social or family problems and female gender increase the risk of depression.
Synthesis 15-13	The risk of post-stroke depression is not associated with brain lesion site. Contrasting data are attributable to the inclusion of aphasic patients in several studies.
Synthesis 15-14	Post-stroke depression increases the short- and long-term mortality rate after stroke.
Synthesis 15-15	Post-stroke depression is a short- and long-term unfavourable predictor of functional recovery.
Synthesis 15-16	Post-stroke depression increases the risk of fall and it is detrimental to quality of life.
Synthesis 15-17	Post-stroke depression is still under-treated, despite evidence in favour of effectiveness of antidepressant drugs also in patients with organic diseases.
Synthesis 15-18	In patients with post-stroke depression, antidepressant therapy may be beneficial to functional recovery but it cannot abolish the detrimental effect of depression on functional outcome.
Recommendation 15.5	Grade C
Recommendation 15.6	Grade C
	*GPP
Synthesis 15-19	Early antidepressant therapy for post-stroke depression is recommended to reduce its detrimental effect on rehabilitation.
Synthesis 15-20	Selective serotonin re-uptake inhibitors are the recommended treatment of post-stroke depression for their favourable tolerability profile.
Synthesis 15-21	The pharmacological therapy of post-stroke depression should be continued for at least 4-6 months.
Synthesis 15-22	Cerebrovascular diseases are associated with an increased risk of cognitive impairment.
Synthesis 15-23	Vascular dementia is the second cause of chronic cognitive deterioration. Cerebrovascular diseases are responsible for 20%-25% of total dementia cases.
Synthesis 15-24	In Italy, prevalent cases of vascular dementia are estimated to be about 150,000.
Synthesis 15-25	In Italy, about 40,000 new cases of vascular dementia are estimated to occur every year.
Synthesis 15-26	Vascular dementia is an unfavourable prognostic factor, because it is associated with increased mortality compared with both the general population and patients affected by degenerative dementias.

Primary risk factors for vascular dementia are:

1. arterial hypertension;
2. age;
3. atrial fibrillation;
4. diabetes mellitus;
5. myocardial infarction;
6. cigarette smoking and alcohol abuse.

Secondary risk factors for vascular dementia are:

1. low educational level
2. ε4 allele of the ApoE gene polymorphism

Neuroimaging predictors of vascular dementia are:

- bilateral, multiple infarctions in the dominant hemisphere and in frontal and meso-limbic areas;
- periventricular and deep white matter lesions.

According to recent diagnostic criteria, the presence of vascular dementia is predicted by cognitive impairment (memory, executive functions, mental flexibility) associated with clinical and neuroimaging signs or symptoms of cerebrovascular disease, possibly temporally related to the onset of dementia.

Assessment of executive functions is recommended in patients with suspected vascular dementia because memory impairment is not the main feature in this dementia type.

Vascular dementia encompasses the following clinical-pathological subtypes:

1. multiple large complete infarcts;
2. strategic single infarcts;
3. small vessels disease;
4. hypoperfusion;
5. haemorrhage.

The different sets of criteria for the diagnosis of vascular dementia are not interchangeable. The highest frequency of diagnosis is achieved with the DSM-IV-TR criteria that are the most inclusive; the lowest with the National Institute of Neurological Disorders and Stroke – Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) criteria, which are the most restrictive.

The Alzheimer's Disease Diagnostic and Treatment Centers (ADDC) criteria together with the Hachinski Ischemic Score (HIS) appear to be the most sensitive criteria for diagnosis of vascular dementia. The National Institute of Neurological Disorders and Stroke – Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) criteria in combination with the Hachinski Ischemic Score (HIS) are the most specific.

According to the Hachinski Ischemic Score the characteristic features of vascular dementia are: fluctuating course, stepwise progression, history of hypertension and stroke, and focal neurological signs.

The Hachinski Ischemic Score is not recommended to be used as exclusive instrument to diagnose vascular dementia.

The concept of Vascular Cognitive Impairment (VCI) has been proposed to include subjects who are affected with a cognitive impairment resulting from cerebrovascular disease but do not completely satisfy the criteria for the diagnosis of vascular dementia.

The term mixed dementia indicates those patients who present an overlapping of criteria for vascular dementia and Alzheimer's disease. According to the NINDS-AIREN criteria, the term mixed dementia should be replaced with that of "Alzheimer's disease with cerebrovascular disease", referring to subjects with a diagnosis of possible Alzheimer's disease associated to clinical and instrumental signs of cerebrovascular disease.

In the acute phase of stroke, the quantification of cognitive impairment is recommended by means of tests that are quick and easy to perform (at the bedside), specific enough to detect neuropsychological deficits following stroke and possibly validated.

The administration of at least the Mini Mental State Examination (MMSE) is recommended to detect a possible cognitive impairment since the acute phase of stroke.

A neuropsychological assessment is recommended if the clinical features and/or the MMSE score indicate one or more cognitive deficits.

A general screening for dementias is recommended if a diagnosis of vascular dementia is made.

Synthesis 15–20

Synthesis 15–21

Synthesis 15–22

Synthesis 15–23

Recommendation 15.7 Grade C

Synthesis 15–24

Synthesis 15–25

Synthesis 15–26

Synthesis 15–27

Recommendation 15.8 *GPP

Synthesis 15–28

Synthesis 15–29

Recommendation 15.9 *GPP

Recommendation 15.10 *GPP

Recommendation 15.11 *GPP

Recommendation 15.12 Grade D

Recommendation 15.13	*GPP	Duplex US examination of supra-aortic vessels is recommended to assess the aetiological and the risk factors of vascular dementia.
Recommendation 15.14	*GPP	Transcranial Doppler is recommended only as a complementary examination.
Recommendation 15.15	*GPP	Use of SPECT or PET, or electrophysiological examinations or cerebrospinal fluid analysis are not recommended for the diagnosis of vascular dementia, unless for scientific researches or for selecting patients in clinical trials.
Recommendation 15.16	Grade A	The search for a mutation of the NOTCH 3 gene is recommended if a diagnosis of CADASIL is clinically suspected.
Synthesis 15–30		Recently it has been suggested to begin the genetic screening starting from exons 3, 4, 11, 19 (with the highest probability of mutation) then sequencing the whole gene if results are negative. A typical mutation – causing insertion or deletion of one cysteine residue – of exon 4 is considered diagnostic in 100% of cases.
Recommendation 15.17	Grade A	The ultrastructural morphologic study of the skin biopsy is recommended in patients with symptoms of CADASIL, because it has a specificity of 100%. It should be performed after the genetic study of the first exons (3, 4, 11 and 19).
Synthesis 15–31		Neuroimaging techniques may be particularly helpful for the diagnosis of vascular dementia because they allow to: <ol style="list-style-type: none"> 1. exclude other causes of cognitive impairment (tumours, severe cortical atrophy, hydrocephalus, etc.); 2. detect cerebrovascular lesions; 3. classify vascular dementia subtypes; 4. provide information for inclusion of patients in controlled clinical trials.
Synthesis 15–32		There is no evidence that the presence of cortical or subcortical territorial or border zone infarcts, and of diffuse white matter changes, found in some cases of dementia, can surely be considered responsible for the cognitive deterioration. In fact neurodegenerative processes, possibly undetectable by neuroimaging, could coexist in these cases.
Recommendation 15.18	Grade A	Cranial CT without contrast or T1- and T2-weighted and FLAIR MRI are recommended for the diagnosis of vascular dementia. Usually the administration of contrast agents is not necessary.
Recommendation 15.19	Grade C	The lack of cerebrovascular lesions on cranial CT or MRI is a significant evidence against the diagnosis of a possible vascular dementia.
Synthesis 15–33		Therapeutic interventions for vascular dementia may be differentiated into: <ol style="list-style-type: none"> 1. primary prevention in subjects with vascular risk factors but no cognitive impairment; 2. secondary prevention in subjects with initial cognitive impairment but not yet demented; 3. secondary prevention and therapy in demented patients; 4. tertiary prevention of complications in patients with severe dementia.
Recommendation 15.20	Grade C	Treatment of hypertension is recommended in all subjects with elevated blood pressure to prevent the occurrence of cognitive impairment. At present there are no comparative data suggesting that a class of antihypertensive drugs is superior to others in preventing dementia.
Synthesis 15–34		Data derived from pharmacological clinical trials suggest that: <ol style="list-style-type: none"> 1. administration of nimodipine improves cognitive functions and the clinical global impression; 2. administration of acetylcholinesterase inhibitors (donepezil, galantamine, rivastigmine) is effective in heterogeneous groups of patients affected by vascular dementia either pure or associated with Alzheimer's disease; 3. none of these drugs significantly improves the independence in the activities of daily living.
Recommendation 15.21	*GPP	Carotid endarterectomy or extracranial-intracranial by-pass are not recommended for the treatment of cognitive impairment due to vascular dementia.
Recommendation 15.22	*GPP	Cognitive rehabilitation is recommended for visuospatial disturbances and neglect following a right-hemisphere stroke.
Recommendation 15.23	*GPP	In the acute and subacute phase of stroke, a speech and language rehabilitation is recommended for treatment of aphasia following a left-hemisphere infarct.
Recommendation 15.24	*GPP	Cognitive rehabilitation is recommended for attention disturbances in the acute phase of stroke.
Recommendation 15.25	*GPP	A formal training on problem solving strategies is recommended for patients with subacute stroke who exhibit an impairment of problem solving when performing the activities of daily living.
Recommendation 15.26	*GPP	At present, the rehabilitation of memory deficits following stroke is not recommended .

