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Abstracts

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Administrative Data and Inverse Occurrence of Cancer and Alzheimer's Disease in Elderly People II: A Misclassification Problem for the Diagnosis of AD

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Background: In a cohort of 115,524 person-years we observed a 40% risk reduction for the occurrence of Alzheimer's disease (AD) in persons with cancer and vice-versa. A relevant concern about these findings is about the potential effect of misclassification in biasing the results.

Methods: All cancer cases were identified from a population Tumor Registry. AD cases were traced from registries of drug prescriptions, hospitalizations and payment exemptions by a classification algorithm that had high specificity but lacked in sensitivity. In the co-occurrence study misclassification of 'exposure' (cancer occurrence in the AD cohort) and of disease (AD in cancer cohort), might be alternatively differential (DM) or non-differential (NDM). A sensitivity analysis was performed in this cohort.

Results: An exposure or disease NDM had the only effect to overestimate the relative risks (RR), weakening the strength of the inverse association. The effect of a DM, unlikely to have occurred, was dependent from levels of sensitivity/specificity in the subgroups of exposure and of disease, and led to biased RR estimates only when classification performances were highly differential.

Conclusions: Large population-based studies on administrative data allow to obtain epidemiological results accounting for possible misclassifications.

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Activation-Related Epileptiform EEG Abnormalities in Population-Based Incident Epilepsy

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Introduction: The utility of activation procedures on multiple EEGs has not been studied in a population-based setting. We assessed the yield of activation-related epileptiform abnormalities on multiple EEGs in a population-based study of incident epilepsy.

Methods: 449 residents of Rochester, Minnesota, with a diagnosis of incident epilepsy and at least one EEG were identified between 1960 and 1994 through the resources of the Rochester Epidemiology Project. The cumulative yield of epileptiform EEG abnormalities was estimated using a life table approach.

Results: Sleep accounted for the greatest proportion of activation-related epileptiform abnormalities, followed by hyperventilation and photic stimulation. Within each activation procedure, the yield was greatest for individuals 1–19 years old at diagnosis. After the first EEG, yield for each activation procedure was compared in people 1–19 years versus ≥20 years at diagnosis. The yield was: 21.6% versus 10.3% for sleep; 6.5% vs. 3.3% for photic stimulation; and 10.3% vs. 5% for hyperventilation.

Conclusions: Sleep showed the highest yield of epileptiform abnormalities compared to photic stimulation and hyperventilation. Within each activation procedure, younger age at diagnosis showed the greatest yield. It may be important to consider sleep to increase the probability of finding an epileptiform abnormality, especially in younger patients.

Prevalence of Cognitive Dysfunction in a Population Based Study in Southern Italy: The GreatAge Study

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Background: Most population based studies on the prevalence of cognitive dysfunction have been conducted outside Italy.

Methods: Subjects over 65 years were recruited in the GreatAge Study in Castellana Grotte, Southern Italy. All subjects underwent a neuropsychological evaluation as part of a multidisciplinary assessment. Global cognitive function, memory, attention, language, executive and visuospatial functions were evaluated using standardized tests. Cognitive performance was considered impaired if less than 2 SDs from the mean of the general population.

Results: We enrolled 514 subjects (312 males and 202 females, mean age of 72.84 ± 6.12 , $6:59 \pm$ education level of 3.63). 50 subjects (10%) were diagnosed as having Subjective Memory Complaints. Cognitive dysfunction was diagnosed in 150 subjects (29.4%). 5.9% ($n = 30$) had amnesic MCI ($n = 13$ single domain impaired; $n = 17$ multiple domains impaired). 23.5% ($n = 120$) had non-amnesic MCI ($n = 83$ single domain; $n = 37$ multiple domains). Visuospatial abilities were impaired in 10.5% of cases, attention in 9.8%, language in 5.3%, and executive functions in 4.3%.

Conclusions: These preliminary results show a higher prevalence of cognitive dysfunction compared to previous studies.

Is There a Connection Between ALS and Cancer?

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Background: We investigated whether patients with ALS have a higher than expected incidence of cancer and how the co-occurrence of cancer modifies ALS prognosis.

Methods: The study population were the 1260 ALS cases incident in Piemonte and Valle d'Aosta in the 1995–2004 period. Only patients with cancers occurring in the 6 months before or after the onset of ALS were included (46 patients). The odds ratio of having a cancer was calculated using as reference the incidence rate of cancers in the same area for the 2004–2006 period (Cancer Registry of Piemonte Region). Odds ratio were calculated by gender and 5-year age-classes.

Results: Cancer in ALS was significantly more frequent than expected in both genders (men, OR 2.01; 99% c.i. 1.15–3.28; women 3.43; 1.78–5.95). The excess of cancers was mostly due to lung cancers (men 4.35, 1.51–9.68; women 4.83, 0.58–14.97) and to breast cancers (6.16, 2.29–13.18). Patients with cancer had a significantly shorter survival than those without cancer ($p = 0.01$); this difference was mainly due to patients with lung cancer.

Conclusions: Cancers, predominantly lung and breast cancers, have an incidence significantly higher than expected in ALS population. Patients with cancer have a worse clinical progression than patients without cancer.

Information Seeking Behavior for Neurological Disorders: An Infodemiological Study of Wikipedia Article Traffic

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Background: Wikipedia is a popular free online encyclopedia used by patients and physicians to search for health-related information. Our aim was to evaluate the Wikipedia page-visits in relation the most important neurological disorders, by determining which factors are related to peaks in Wikipedia searches for these conditions.

Methods: Wikipedia articles related to ten different neurological disorders were considered. We analyzed information regarding the total article views for ninety days and the rank of these articles among all those available in Wikipedia. We determined the highest search volume peaks to identify possible correlation with online news headlines.

Results: No relation between incidence or prevalence of neurological disorders and the search volume for the related articles was found. Seven out of ten neurological conditions showed correlations in search volume peaks and news headline. All these seven peaks were related to news about famous people suffering from neurological disorders, especially those from show business.

Conclusions: Identification of discrepancies between disease burden and health-seeking behavior on Wikipedia is useful in the planning of public health campaigns. Celebrities who publicly announce their neurological diagnosis might effectively promote awareness programs and increase public knowledge and reduce stigma related to diagnoses of neurological disorders.

Predicting the Rate of Cognitive Progression in Alzheimer's Disease: Data from The ICTUS Study

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Background: Different rates of cognitive progression have been observed among Alzheimer's disease (AD) patients. The present study aimed at evaluating whether the cognitive course of AD may be predicted by widely available and easy-to-assess factors.

Methods: Data are from AD patients recruited in the ICTUS study. Multinomial logistic regression analysis was performed to measure the association between several socio-demographic and clinical variables and 3 different progression rates defined by modifications (after one year of follow-up) of the MMSE score: 1) 'slow' progression, decrease of MMSE score ≤ 1 point; 2) 'intermediate' progression, decrease of MMSE score between 2 and 5 points; and 3) 'rapid' progression, decrease of MMSE score ≥ 6 points.

Results: A total of 1,005 patients were considered for the present analyses. Overall, most of the study participants exhibited a slow cognitive decline. Higher ADAS-Cog scores at baseline were significantly associated with both 'intermediate' and 'rapid' progressions after 12 months. Conversely, increasing age was negatively associated with 'rapid' cognitive progression.

Conclusions: Predicting the course of AD may have important practical implications both in clinic and research settings. The influence of age and baseline cognitive impairment should always be carefully considered when designing AD trials and defining study populations.

Amyotrophic Lateral Sclerosis with Comorbid FTD: A Possible Role of Cognitive Reserve

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Background: ALS patients may display frontotemporal dementia (ALS-FTD), executive (ALS-ECI), non-executive (ALS-NECI) and behavioral impairment (ALS-Bi). Cognitive reserve (CR) seems protective against pure FTD. Data about ALS-FTD are lacking.

Methods: 183 Piedmontese incident cases (2009–2011) constituted our discovery cohort (DC). The validation cohort (VC) (n = 113) included Piedmontese incident cases (January 2012 – June 2013) and other patients diagnosed in that period. Subjects underwent neuropsychological and genetic testing. A Reserve Index (RI) (2–12) was calculated from education and occupation.

Results: In the DC, 49.7% were normal, 12.6% ALS-FTD, 19.7% ALS-ECI, 5.5% ALS-NECI, 6.0% ALS-Bi, 6.0% non-classifiable (ALS-NCCI). In the VC, 50.5% were normal, 15.9% ALS-FTD, 18.6% ALS-ECI, 3.5% ALS-NECI, 6.2% ALS-Bi, 5.3% ALS-NCCI. In the DC, ALS-FTD patients had lower education (4.7 years, SD 1.9) and RI (4.9, SD 1.3) than other groups ($p = 0.0001$). In the VC, ALS-FTD patients (7.0 years, SD 2.6) had equal education of ALS-NECI (7.0, SD 1.4), that was lower than other groups ($p = 0.003$). ALS-FTD patients had lower RI (5.7, SD 1.6) than other groups but ALS-NECI ($p = 0.003$). Results were independent from sex, age, onset site and were confirmed among *c9orf72*-mutated patients ($p = 0.012$).

Conclusions: CR may act in ALS-related frontotemporal syndromes, primarily full-blown FTD, including *c9orf72*-mutated cases.

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Pre-Stroke and Follow Up Neuropsychiatric Profile in Patient Affected by Post-Stroke Dementia

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Background: Several studies indicate that stroke increases the risk of dementia. Data about pre-stroke neuropsychiatric disturbances in patients affected by post-stroke dementia (PSD) are lacking. The aim of this study is to examine the neuropsychiatric profile of patients with dementia before and after a cerebrovascular event.

Methods: Pre-stroke neuropsychiatric disturbances were assessed at baseline, at three months ($n = 145$) and one year ($n = 132$) after a cerebrovascular event. Patients with PSD were compared to patients not experiencing dementia (Post Stroke No Dementia, PSND).

Results: Compared to the PSND group, patients with PSD showed a higher NPI (Neuropsychiatric Inventory) total score at three months (13.0 ± 10.1 vs 7.6 ± 8.5 ; $p < 0.001$) and at one year after the cerebrovascular event (11.5 ± 7.3 vs 6.9 ± 5.6 ; $p < 0.001$). This score reflects a greater level of apathy in the PSD group than in the PSND group (3 months: 2.1 ± 2.5 vs 0.5 ± 1.3 ; $p < 0.001$ – one year: 3.1 ± 3.4 vs 1.1 ± 1.8 $p < 0.001$).

Conclusions: These findings identify the importance of investigating pre-stroke neuropsychiatric profile, in order to define the burden of psycho-behavioral disturbances in patients affected by pre and post-stroke dementia.

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New Onset of Dementia or Previous Cognitive Impairment: A 3-Month and 1 Year After Stroke Overview

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Background: Stroke is an important risk factor for dementia, but the exact mechanisms involved in cognitive decline remain unclear.

Methods: Baseline cognitive, functional and behavioral profile, clinical variables at onset of symptoms and neuroradiological hallmarks (medial temporal lobe atrophy, MTLA) were compared between two groups (Post Stroke Dementia, PSD vs. Post Stroke No Dementia) at 3 months (114 subjects) and 1 year (105 subjects) after the acute cerebrovascular event.

Results: In a logistic regression model, older age ($p < 0.05$), education ($p < 0.05$), prestroke Informant Questionnaire (IQ) code ($p < 0.05$), premorbid apathy ($p < 0.05$), and MTLA ($p < 0.05$) were independently associated with PSD at 3 month after a cerebrovascular event, while at 1 year older age ($p < 0.05$), prestroke IQ code ($p < 0.05$), MTLA ($p < 0.05$), Acute Physiology and Chronic Health Evaluation II (APACHE II) ($p < 0.05$) were independently associated with PSD.

Conclusions: cognitive impairment after stroke may not only be a consequence of the cerebrovascular event but also follows the type of neurodegenerative pathology.

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Prestroke Dementia: Characteristics, Clinical Features and Primary Outcomes of in Consecutive Series of Patients

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Background: The pre-stroke level of cognitive function should be taken into account in order to predict the impact of stroke on the subsequent risk of dementia. The aim of the present study was to investigate the presence and correlates of pre-stroke dementia (PSD) as well as to identify its clinical features and the influence of pre-stroke cognitive impairment on primary outcomes.

Methods: Baseline cognitive, functional and behavioral variables and neuroradiological hallmarks (medial temporal lobe atrophy, MTLA) were compared between these two groups. (Post Stroke Dementia vs Post Stroke Non Dementia). Primary Outcomes (Barthel, IADL, NIHSS discharge, Rankin scale discharge and mortality) were analyzed according to the presence/absence of PSD.

Results: Premorbid cognitive impairment (IQcode) was independently associated with worsen NIHSS at discharge (OR 0.3), follow up IADL (1.4) and higher mortality (OR 5.3). Age and comorbidity (number of disease) were independently associated with impairment of IADL during follow up. Age (OR 1.0) and comorbidity (OR 1.0) were uneventful.

Conclusions: Pre stroke dementia could be defined as a primary risk factor for a worse functional outcome in patients with acute cerebrovascular event.

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Cochrane Textbook of Neurology

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Background: The Cochrane Neurological Field decided to codify the amount of published neurological work in the Cochrane Library in a *Textbook* with the aim to provide a straightforward way to reach new audiences with diverse educational backgrounds, socio-economic resources and priorities for research.

Methods: Every three months since 2007, CNF has highlighted Reviews of Neurological interest published or updated in the Cochrane Library. Reviews are blindly selected by two neurologists with different background; each appropriate title is ascribed to a topic within the 'Index'.

Results: The *e-book of Neurological Cochrane Reviews* has titles and chapters, it's possible to 'turn the pages' of the categorized reviews, each title has a direct link to an abstract and a plain language. Within each category there are more specialized sub-categories. Reviews of 'shared interest' between disciplines are enhanced. The ten most read and appreciated reviews are highlighted.

Conclusions: The Cochrane Textbook of Neurology will disseminate the efficacy of interventions discovered in the literature in this field. Comments and evaluations by readers are encouraged, essential to maintain the vital involvement of clinicians, decision makers and consumers. This Cochrane product is publicized on: www.cnfbook.org and www.cochrane.neuronet.org.

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Hospitalization for Stroke in the Aosta Valley Region, Italy. Analysis of the First-Admission Discharge Data from 2000 to 2012

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Background: Analysis of first admission for acute cerebrovascular disease with specific ICD9CM codes in hospitalization discharge data provide a useful and easily consultable in-house means of monitoring stroke outcomes, obviating the need to retrieve the data reported in the community-based stroke registry.

Objective. To use discharge records to evaluate trends in hospitalization and mortality rates for stroke further to planning community-wide patient management.

Methods: We analysed the Aosta Hospital discharge records of inpatient admissions listing stroke as first diagnosis and ICD9CM codes 430, 431, 433.x1, 434 and 436.

Results: We registered 3524 cases. Of these, 586 (18%) were haemorrhagic (430 subarachnoid haemorrhage = 4%; 431 intracerebral haemorrhage = 14%), and the remaining 2938 (82%) were ischemic. The rate of first-hospitalization decreased by –32% ($R^2 = 0.77$, $p < 0.001$) over the monitoring period. The decline in admissions was observed in all age groups, across all stroke types, and in both sexes. Correspondingly, the death rates fell by –63% ($R^2 = 0.81$, $p < 0.001$).

Conclusion: The observed decline in hospitalization and mortality rates may reflect an increased awareness and improved control of vascular risk factors and a general improvement in acute stroke care in the Region. Hospital discharge records are an valuable source of information for in-house care monitoring.

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Outcomes and Characteristics of Patients Hospitalized for Stroke in the Aosta Valley Region, Italy. Analysis of the Hospital Discharge Data from 2000 to 2012

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Background: Hospital discharge data could be used as a rapid in-house source of information for monitoring stroke patient outcomes in order to planning community-wide patient management strategies. We aimed to evaluate changes in the outcomes and characteristics of patients hospitalized for stroke, using discharge records.

Methods: We analysed the records of 3524 inpatients whose first-listed diagnosis was stroke (ICD9CM codes 430, 431, 433.x1,

434, 436) discharged from the Aosta Hospital in North-Western Italy.

Results: Although the mean age, gender ratio, and stroke types remained relatively stable between 2000 to 2012, the hospitalization and mortality rates decreased by -32% and -63%, respectively, the average length of stay fell by -29%, from 26.2 to 18.6 days. Proportions of discharge status (at home 65%, deceased 19%, referral to long-term care institution 13% and short-term hospital 3%) and comorbidities (diabetes 5%, hypertension 17% and atrial fibrillation 10%) remained stable.

Conclusions: The observed decline in stroke mortality, despite little change in patient characteristics, may reflect a reduction in stroke severity due to better control of vascular risk factors as well as a general improvement in acute care. Similar analyses of discharge data may be used to monitor the efficacy of patient care over time.

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Parkinsonism Prevalence Estimate Using Drug Prescription Archives in a Region of Central Italy

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Background: Estimates of the prevalence of parkinsonisms vary largely across studies and countries. We used prescription records of medications for parkinsonism to estimate the prevalence of this condition.

Methods: Retrospective survey based on the Lazio regional drug registry, collecting routinely all drug prescriptions. Cases of parkinsonism were defined as those who received a medication for parkinsonism (dopamine or dopamine derivatives and/or monoamine oxidase B inhibitors) for at least 6 months in a 5-year period (2005–2009). Crude and standardized prevalence rates for 2009 were calculated, considering all cases treated in the index month.

Results: Overall and standardized prevalence rates of parkinsonism in Lazio were respectively 283/100,000 (95% CI: 278–287) (292 in men and 274 in women), and 294/100,000 (95% CI: 289–298). The highest overall prevalence rate was observed among people aged 85–89 years (246/100,000), while the lowest in subjects aged <65 (38/100,000). Prevalence rates in people 65+ and 75+ years were respectively 1.3% and 1.9%.

Conclusions: The use of a regional drug registry based on currently available health information systems may be a suitable method to estimate the prevalence of parkinsonism. Providing an accurate estimate of its prevalence is essential for public health programming.

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From the Survey of Dedicated Services to the Observatory for Dementias in Italy

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Background: The aim of this survey is to build a reasoned and dynamic map of health and social health services available in Italy for dementia.

Methods: The survey started on February 2014 and will last until August 2015. All available services will be identified in collaboration with the regional referents; information will be gathered through standardized forms based on structure, process and outcome indicators, and a dynamic map of services along with a website on dementias will be created.

Results: About 2000 services have been identified up to September 2014: 523 Alzheimer evaluation units (AEUs), 775 daytime centers, and 691 residential structures. Standardized forms specific for each type of structure were delivered starting from June 2014. The first 67 of the 138 forms sent to the AEUs were returned starting from September 2014.

Conclusions: The survey will be carried out by the ISS with funds from the Ministry of Health (CCM), and will start one of the core actions of the National Dementia Plan. This is the first national survey of all health and social health services for dementia. The Observatory for Dementias through its website (www.iss.it/demenze) will provide a dynamic map of services.

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An Appropriate use of MRI in Multiple Sclerosis

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Magnetic resonance imaging (MRI) has become an indispensable tool for the diagnosis and monitoring of multiple sclerosis (MS). In addition to ruling out other possible diseases that can mimic the clinical characteristics of the disease, brain and spinal cord MRI provides evidence of clinically undetectable disseminations in space and time of MS, leading to an early and definite diagnosis. In the therapeutic area, the high sensitivity of MRI in recognizing MS lesions and their changes over time qualifies this method as a standard surrogate measure in all trials designed to evaluate the efficacy of new experimental drugs. In recent years, the systematic application of non-conventional MRI techniques in the evaluation of the natural history of MS has also made it possible to obtain a better characterization of the underlying pathological processes, and to improve the degree of correlation between

clinical manifestations and imaging findings. The application of MRI in the study of MS has demonstrated the need for a multi-parametric approach, to be adapted to the stage of the disease and the mode of action of therapeutic agents.

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Epidemiology of Organizational Features of Multiple Sclerosis Centers in Italy

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Background: There is an increasing debate on the structure and organization of multiple sclerosis (MS) centers, yet there are no national data on MS centers in Italy. Agorà is a multicenter, retrospective observational study focused on the care of MS in Italy. Here we present the results on structural and organizational features of MS centers in Italy.

Methods: In 2011, a questionnaire was administered to the directors of MS centers in Italy in order to explore the number of patients followed by the centers, and a number of structural and organization features.

Results: Out of 193 existing MS centers, 112 (58%) participated (Northern Italy 50%, Central Italy 22.3%, Southern Italy 28.6%). A relapsing-remitting form was present in 37,370 (67.7%) patients. 72% of centers have collaborations with a psychologist, 60% with an ophthalmologist, urologist, physiotherapist, and 45.5% with a psychiatrist and gynecologist. Only 22% of centers have a clinical-diagnostic pathway formalized for patients with MS. Only 15.3% of centers provide integrated home care.

Conclusions: Our study shows that among MS centers in Italy there is a great variability in organizational features. A need for guidelines on this matter is urgent in Italy.

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Stroke Due to Cardiac Embolism. Not Only Atrial Fibrillation

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Introduction: The etiological stroke classification is essential for correct treatment in the acute and post-acute phase and in sec-

ondary prevention. Ischemic strokes are due to: Large Artery Atherosclerosis (LAA), Cardiac Embolism (CE), Small Vessel Disease (SVD), Other Causes (OTH), Undetermined (UND) (ASCO classification). Non-valvular-atrial-fibrillation (NVAf) is the main cause of CE, but other diseases may be involved.

Methods: In order to identify the relevance of other causes of CE, we exhaustively analyzed an unselected stroke population with the ASCO method.

Results: We studied 760 ischemic strokes: 299 CE (39%); 202 LAA (27%); 117 SVD (16%); 56 OTH (7%); 86 UND (11%). In CE we observed 74 (25%) patients with a cause other than NVAf. In 16 (5%) AF was also evident. Finally, 58 subjects had cardiac CE without AF.

Conclusions: The principal cause of stroke was CE (39%), mainly due to NVAf (75%), but other diseases played a causal role in 25%, in order of frequency: PFO, cardiac valve pathology, acute myocardial infarction, dilated cardiomyopathy, interventional procedure or surgery, atrial myxoma, sick sinus disease. The patients with CE not due to NVAf were younger and more often male than the group with NVAf.

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Drug-Resistant Epilepsy in a Well-Defined Population of Northern Italy

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Introduction: Drug-resistant epilepsy (DRE) is defined by the International League Against Epilepsy (ILAE) as a failure of adequate trials of two tolerated, appropriately chosen and used anti-epileptic drugs. The percentage of DREs is 15–20% in well-defined populations. There are few published reports on the prevalence and no reports on the incidence of DRE. Our aim was to calculate prevalence and incidence of DRE in a well-defined population of Northern Italy using the ILAE definition.

Methods: The study population (146,506; year 2008) resided in the province of Lecco. 122 general practitioners were contacted to identify residents during the period 2000–2008 fulfilling the diagnosis of active epilepsy (at least one unprovoked seizure and/or treated within the past 5 years). All patients received neurological confirmation.

Results: During the study period, the percentage of DREs was 16.2% (106/656) in the total epilepsy population and 11.4% (37/326) among incident cases. The point prevalence (December 31, 2008) and incidence were respectively 0.72 per 1,000 and 3.1 per 100,000/year.

Conclusions: In line with previous reports, 1/6 patients with active epilepsy in the general population have DRE. About 1/10 patients with newly diagnosed epilepsy will develop DRE in a nine-year period.

The Anticholinergic Cognitive Burden of Drugs in the REMIND Cohort: A Cross-Sectional Study in Elderly People with Cognitive Complaints

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Background: An Integrated Care Pathway (ICP) for dementia was approved by the Lombardy Region Health Office and operationalized by the Milan Health Authority. The REMIND study is a 3-year population-based prospective cohort study in Milan which aims to implement the ICP.

Methods: From April 2013 to March 2014, 4318 subjects with cognitive complaints underwent the MiniMental State Examination (MMSE) administered by 336 General Practitioners (GPs). Drug history was collected and the ACB was scored. Aim. To evaluate the anticholinergic cognitive burden (ACB) of drugs in the cohort of the REMIND study.

Results: Out of 4318 subjects, 1119 (26%) received at least one drug with anticholinergic action: 965 (86%) with ACB score 1 and 154 (14%) with ACB score 2. The mean MMSE score (range 0–30) decreased with the increase of the ACB score: 26.1 score 0 vs 25.7 score 1 vs 25.2 score 2; $p < 0.0001$.

Conclusions: This is the first study that investigated the ACB of drugs in elderly people referring to GPs for cognitive complaints. The widespread use of drugs with anticholinergic action was found to be inversely related to cognition. From a public health perspective this finding could have wide implications in order to implement prevention strategies.

The Incidence of Multiple Sclerosis in the Province of Ferrara, 2004–2010: The Emilia Romagna Multiple Sclerosis Registry (ERMeS)

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Background: The province of Ferrara, Emilia Romagna Region, has featured increasing frequency of multiple sclerosis (MS), similarly to what reported in other Mediterranean populations. We aimed to update incidence trends in the same study area, to inves-

tigate on the diagnostic delay and on age groups at higher risk for disease onset in a population with relatively stable demographic features.

Methods: A community-based incidence study was conducted in the province of Ferrara (350,000 mean pop ca.), and individuals with clinical onset related to MS (Poser criteria) between 2004 and 2010 were included.

Results: The average crude annual incidence based on 181 MS patients (53 men and 128 women) was 7.27 per 100,000 (95% CI 6.27–8.43), 9.86 (95% CI 8.26–11.76) in women and 4.44 (95% CI 3.33–5.82) in men. Incidence tended to increase from 2004 to 2010, peaking in the period 2007–2010 with 7.33. The highest rate of 21.36 per 100,000 was found for age 25–29.

Conclusion: Previous studies in the province of Ferrara showed stable incidence rates in the period 1965–1989. An increasing trend was observed in 1990–2003 and we now show a further increase in the next quinquennium. An older age of MS onset is being recorded.

Physical Activity, and Physical Activity Related to Sports, Leisure and Occupational Activity as Risk Factors for ALS: A Systematic Review

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Background: The etiology of amyotrophic lateral sclerosis (ALS) is considered multifactorial and probably due to an interaction between environmental and genetic factors. The objective of this systematic review is to provide a comprehensive overview of all available evidence on physical activity (PA) as a potential risk factor for ALS.

Methods: All relevant literature published up to April 2014 was gathered through bibliographic searches on PubMed, The Cochrane Library, Embase and SciSearch. All studies reporting PA as the exposure of interest and a diagnosis of ALS or motor neuron disease (MND) were selected. Included studies were assessed using the Newcastle-Ottawa Scale (NOS) for quality assessment of non-randomized studies.

Results: Bibliographic searches yielded 1496 records. Eighteen case control studies and 7 cohort studies were included in the analysis. Evidence on PA as a risk factor for ALS remain inconclusive, but most of the cohort studies reported a significantly higher number of cases in professional soccer and football players.

Conclusions: To our knowledge, this is the first systematic review including all studies investigating PA and participation in sports as potential risk factors for ALS. Included studies were highly heterogeneous, thus preventing the direct comparison of data.

Incidence and Prevalence of Multiple Sclerosis in Sardinians, Insular Italy: An Update

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Background: Sardinia, insular Italy, is a high-risk area for multiple sclerosis (MS) with increasing temporal trends. We have updated MS prevalence and incidence estimation.

Methods: Patients with MS according to Poser criteria were included. The study was conducted in northern Sardinia, in the province of Sassari till 2004, and in the provinces of Sassari and Olbia-Tempio in 2005–2009. Multiple epidemiological sources were used.

Results: MS mean crude incidence rate for 1965–2009 increased from 1.81 per 100,000/year (1.42 in men, 2.19 in women) to 8.39 (4.48 and 12.18) with a F:M from 1.54 to 2.72. Incidence peaked in 2000–2004: 10.80 (95% CIs: 8.61–12.99), 6.39 (95% CIs: 5.32–7.46) in men and 15.04 (95% CIs: 13.09–16.98) in women (F:M ratio of 2.35). On prevalence day, 31 December 2009 the total crude MS prevalence was 260.4 per 100,000 (95% CIs: 256.4–264.4), 145.6 (95% CIs: 143.5–147.7) in men and 371.3 (95% CIs: 367.9–374.7) in women (F:M ratio of 2.55). The mean incidence of pediatric onset MS was 0.56 per 100,000/year in 1965–1999.

Conclusion: Sardinians are still found at very high and increasing risk for MS. Incidence of pediatric MS in Sardinians appears to be higher than reported elsewhere.

Acknowledgements: Regione Autonoma della Sardegna, Assessorato dell'Igiene e della Sanità.

Incidence and Prevalence Trends of Myasthenia Gravis in the Sardinian Population, Insular Italy

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Background: Over the last fifty years there has been a clear trend towards an increase of the reported prevalence of myasthenia gravis (MG). In Sardinia a prevalence of 11.1 per 100,000 in 1994 and mean incidence rate of 0.8 per 100,000/year in 1982–1994 were reported. We aimed to update MG incidence and prevalence estimates in Sardinians and compare them with previous reports.

Methods: Patients with diagnosis of MG according to clinical criteria, electrophysiologic and laboratory findings (anti-AchR

and MUSK antibodies) were included. The study was conducted in the provinces of Sassari and Olbia-Tempio, northern Sardinia, for the period 1996–2010. Multiple sources of information were used and data deduplicated for statistical analysis.

Results: On prevalence day (December 31, 2010) 320 MG cases were living in the study area. The overall crude prevalence was 64.9 (95% confidence interval, CI, 61.0–68.9) per 100,000 pop (1.08 men:women ratio). The mean annual incidence rate was 4.60 (95% CIs 1.77–7.43) per 100,000 (men:women ratio of 1.05).

Conclusion: A relevant increase in MG incidence and prevalence was observed in northern Sardinia over the past three decades, placing this area at high risk for the disease. MG incidence and prevalence increased in women, and late-onset MG predominantly in men.

Pre-Eclampsia Is Associated to Probably Symptomatic Epilepsy in the Adults

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Background: Pre-eclampsia is a risk factor for childhood epilepsy, but whether such risk remains high in adulthood is unclear.

Methods: A retrospective cohort study of 3374 live newborns in the city of Sassari, insular Italy was carried out between 1 January 1980 and 31 December 1983. The cohort was followed from birth until 1 April 2010. Perinatal exposures were defined and a diagnosis of non-symptomatic epilepsy at age 18 years and older was used as outcome.

Results: 89/3374 (2.8%) children had been exposed to pre-eclampsia; of these, 32 received a diagnosis of epilepsy during the follow-up. The incidence of epilepsy among the exposed to pre-eclampsia was 1.5 per 1000 vs. 0.3 among the non-exposed, with rate ratio (IRR) of 5.44 (95% CI: 1.9, 16.7). Forceps delivery was performed in 3.2% of children developing epilepsy vs. 0.1% of all births. Smoking during mother's pregnancy and use of drugs during labour were also more frequent among children who developed epilepsy. No differences in the mean Apgar Score, nor correlation with birth weight was observed.

Conclusion: Pre-eclampsia and delivery modalities were found associated to a higher risk for epilepsy in early adulthood. A predisposing epileptogenic effect of perinatal factors on the developing brain is hypothesized.

Multiple Sclerosis and Exposure to Dietary Intake of Vitamin D During Adolescence in An Italian Population: The EnvIMS Study

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Background: Vitamin D (vitD) has a key role in immune-mediated disease pathogenesis, including MS. We explored the effect of teenage exposure to vitD-rich diet within the international multicentre case-control study of environmental risk factors in MS (EnvIMS Study).

Methods: An ad hoc postal self-administered questionnaire was used to record exposure to food items at teenage. In collaboration with a nutritionist, the intake of vitD was estimated per portion of food and frequency of intake.

Results: Among 1991 Italian participants (684 cases, 1307 controls) an inverse association was found between MS and consumption of fish (OR = 0.80; 95% CI 0.65–0.97), especially anchovies, sardines and mackerel (adjusted for sex, smoke habit, sun exposure and vitD-supplementation). Consumption of smoked meat (OR = 0.74; 95% CI 0.58–0.95) and yoghurt (OR = 0.80; 95% CI 0.65–0.98) was also associated to lower risk for MS. A higher overall estimated mean intake of vitD was reported for controls vs cases.

Conclusion: MS was found associated to teenage low exposure to vitD-rich food in Italian participants to the EnvIMS Study, as compared to the control population. The potential relevance of age-specific vitD intake through diet to prevent immune-mediated diseases is hypothesized.

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The Disease Natural History of Multiple Sclerosis in the Republic of Moldova

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Background: No epidemiological studies are reported for Multiple sclerosis (MS) in Moldovans. We aimed to analyse the

distribution of clinical data at onset and at the prevalence day (31-12-2012) in the Republic of Moldova.

Methods: MS was diagnosed according to 2010 McDonald Criteria. Information was collected on clinical course, and signs, symptoms and Expanded Disability Status Scale (EDSS) at onset and at the last neurological examination.

Results: The analysis of clinical data was possible for 464 patients among the 747 prevalent in the study area. Mean (SD) diagnostic delay was 3.0 (4.9) years (CI 95%, 2.6–3.5; median: 1 year; range 0–31 years). Mean (SD) disease duration from clinical onset to prevalence day was similar in men, 8.44 (7.22) years, and women (9.54, 7.82). The clinical course at onset, retrospectively assessed, was RR in 419 patients (89.7%) and progressive in the remaining. The most frequent symptoms at onset were pyramidal (55.6%), sensory (31%), brainstem (26.1%) and visual (24.6%). EDSS score at prevalence day was available for 469 patients: it was 0–3.5 in 267 (56.9%), 4–6.5 in 173 (36.9%), and 7–9.5 in 29 (6.2%).

Conclusions: It is interesting and relevant to investigate the disease natural history in this population, since it is almost not influenced by the use of disease-modifying drugs.

Bulbar Subscore of ALSFRS-R at First Examination and Slope of Bulbar and Respiratory Subscores During Follow-Up Are the Strongest Predictive Factors for Survival in ALS Patients

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Background: We evaluated the predictive power of single items or the subscores of the ALSFRS-R at the first examination and their slopes during the follow-up period for survival in patients with Amyotrophic Lateral Sclerosis (ALS).

Methods: Patients with ALS followed up at our Centre and with correct information on the primary endpoint (death or tracheostomy) were included. Each item of the ALSFRS-R at first examination and during follow-up were recorded to assess their effect on survival. Univariate and multivariate Cox Model (CM) was used to identify single items (or group subscores) correlated with survival.

Results: The study included 178 patients (59 women), with mean disease duration of 12 (±9.2) months. No single item of the ALSFRS-R scale at first examination was associated with survival. In multivariate CM, only bulbar subscores were significantly associated with survival ($p < 0.05$, HR 0.932 [95% CI 0.869–1.000]). Considering the slope of subscores during follow-up, bulbar and respiratory subscores were significantly correlated with survival.

Conclusions: The ALSFRS-R bulbar subscore at first examination and the slope of bulbar and respiratory subscores during follow-up have the strongest association with survival.

Multiple Sclerosis Progression Is Not Associated with Birth Timing in Italy

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Background: Month of birth has been associated in some studies with the susceptibility to develop Multiple Sclerosis (MS). However, only few studies have evaluated whether birth timing also affects disease progression. The aim of this study is to assess whether season and month of birth are associated with disease progression in a large cohort of Italian patients.

Methods: A total of 1866 Italian MS patients, diagnosed according to Poser and McDonald criteria, were consecutively ascertained from 1996 through 2011 by two Italian Consortia, PROGEMUS and PROGRESSO. Patients who were born in Sardinia, outside Italy and with non-Italian ancestry were excluded (n = 84). Quantile regression was used to analyze the impact of each month and season of birth with all the others combined on the median Multiple Sclerosis Severity Score (MSSS).

Results: We analyzed 1782 patients, with a mean age at onset of 32 years (SD: 10.4), and a mean disease duration of 8.8 years (SD: 7.8). The overall median MSSS score 3.86 (CI: 3.55–4.14): 7.36 (CI: 6.98–7.65) for Primary Progressive and 3.19 (CI: 2.93–3.45) for Bout Onset. No significant temporal trend was found after adjustment for multiple comparisons.

Conclusions: Birth timing shows no association with MS progression in Italian patients.

Advance Directives and Palliative Care in ALS Patients: The Experience of an Epidemiological Register

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Background End-of-life care is an important aspect of ALS management. The aim of this study is to evaluate the diffusion of advance directives (ADs) and the use of palliative care services (PCS) in a population-based series.

Methods: We included all the 217 patients resident in province of Turin, Piedmont, Italy, diagnosed in the 2008–2010 period. Data on discussion of ADs, cause and place of death and PCS activation were recorded.

Results: On June 1st, 2014, 183 (84%) patients were dead and 34 (16%) alive. ADs were discussed with 103 patients (54% of dead/tracheostomized patients). At time of discussion, patients had a median ALSFRS score of 21 [IQR 16–30] and a median MITOS Stage of 2 [IQR 1–3]; ADs were fulfilled in 90% of cases. Gender, education, and marital status did not influence discussion and disposition of ADs, while patients <60 years more frequently chose tracheostomy (p = 0.004). PCS support was activated for 47 patients (55% of those refusing tracheostomy). Patients opting for tracheostomy survived more (mean survival 2.2 years [SD 0.7]) than those who received tracheostomy on emergency basis (0.7 years [SD 1.0]).

Conclusions: Further efforts are needed to improve diffusion of ADs and PCS among ALS patients.

Are Arterial Hypertension and Diabetes Modifiers of ALS Phenotype and Outcome? A Population-Based Study

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Background: Several studies have assessed vascular risk factors in ALS. Pre-morbid arterial hypertension (AH) has been reported to shorten survival in ALS patients while diabetes mellitus type II (DM) delays the onset of motor symptoms.

Methods: We included all 712 incident ALS patients in the 2007–2011 period in Piemonte region (323 women and 389 men, mean age at onset 66.7 years [SD 10.7]) and retrospectively investigated the presence of AH and DM.

Results: 314 patients (44.1%) had AH for at least 2 years before the onset of ALS, and 68 (9.6%) had DM. Patients with AH were significantly older (men, 68.4 [9.0] vs. 64.8 [11.4]; women 70.4 [8.5] vs. 64.0 [11.6]; $p = 0.0001$ for both). Pre-morbid AH or DM did not influence site of onset (bulbar vs. spinal). The mean age at onset did not differ between patients with and without DM (men, 67.9 [8.8] vs. 66.1 [10.8]; women, 68.7 [8.7] vs. 66.9 [10.9]; $p = n.s.$ for both). Survival from onset was slightly reduced in women ($p = 0.05$) but not in men with AH, and was not affected by the presence of DM.

Conclusions: Phenotype and survival of ALS patients are not affected by pre-morbid AH or DM.

Multiple Sclerosis in the Republic of Moldova: An Epidemiological Study of Prevalent Cases

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Background: Prevalence of multiple sclerosis (MS) in Eastern Europe has been reported to range from 21 to 83 per 100,000 population. No data exists on MS prevalence in Moldovans, an ethnicity sharing features with Romanians, Russians and Ukrainians. This study aims to describe age and gender-specific prevalence of MS in the Republic of Moldova (population: 3,559,541).

Methods: 747 MS patients, diagnosed according to 2010 McDonalds Criteria were ascertained through different epidemiological sources, including medical hospital records and population health statistics.

Results: 747 patients were residing in the study area on the prevalence day (31-12-2012), yielding a crude onset-adjusted prevalence of 21.0 per 100,000 (95% CI: 14.8–27.1) and 20.2, standardized to the European population. Sex was known for 724 patients: 460 women (63.5%; mean age 42.1 ± 11.9 years) and 264 men (36.5%; 40.8 ± 12.8). The highest estimates were in the age group 40–49, 57.0 and 29.0 per 100,000 for women and men. A higher number of MS patients was recorded in the rural (72.6%) than in the urban area (27.4%).

Conclusions: This is the first population-based prevalence study of MS conducted in the Republic of Moldova, based on multiple data sources. MS was found to be rarer than on average in Europe.

Ethnic Differences in Incidence of Amyotrophic Lateral Sclerosis

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Background: Amyotrophic Lateral Sclerosis is a rare neurodegenerative disorder with a high personal, societal and economic burden. Whether ALS incidence varies with ethnicity is of major interest.

Methods: We performed a systematic review and meta-analysis of data concerning the differences in phenotype and outcome of ALS as regard ethnicity. We aimed to produce synthesized epidemiological indicators.

Results: This review displays pooled and weighted estimates of ALS crude and standardized incidence of worldwide population-based studies. Based on a continental approach, significant differences have been reported between Europe and East Asia (China, Japan), South Asia (Iran) and West Asia (Israel). Conversely, homogeneous rates have been reported in Caucasian populations from Europe, North America and New Zealand. A more refined approach involving genomic data confirmed the positive association between ALS incidence and European ancestry and the negative association between ALS incidence and Asian ancestry or admixed populations.

Conclusions: This review sets the scene to sustain a collaborative study involving a wide international consortium in order to perform, with homogeneous methodology, an investigation of the link between ancestry, environment, and ALS incidence.

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Ethnic Differences in Phenotype and Outcome of Amyotrophic Lateral Sclerosis

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Background: Race and ethnicity might modulate disease via genetic background. Knowledge on how ethnicity modifies ALS phenotype may provide important insight into the risk factors and pathogenic mechanisms of the disease.

Methods: We performed a systematic review and meta-analysis of the data concerning the differences in phenotype and outcome of ALS as regard ethnicity.

Results: The results highlight the ALS phenotypic heterogeneity at time of onset (age, sex ratio (SR), bulbar onset), of diagnosis (age, definite ALS according to El Escorial criterion), in early follow-up (ALS-plus comorbidities), and late follow-up (survival). A major explanatory variable of the variability of ALS phenotype is sub-continent. Some markers of ALS phenotype had homogeneous distribution in western countries (SR, mean age at onset/diagnosis) but their distribution in other subcontinents was remarkably different. Other markers presented variations even in European subcontinents, (fALS, bulbar onset, definite ALS) and in other continents. ALS outcome strongly varied, with a median

survival time since onset ranging from 24 months (North Europe) to 48 months (South Asia).

Conclusions: This review sets the background for a collaborative study involving a wide international consortium to perform with a standard methodology an investigation of the link between ancestry, environment, and ALS phenotype.

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Comparative Analysis of Mental Workload in Laparoscopy and Open Surgery

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Background: The mental resources required to the laparoscopic surgeon could be higher compared to other surgeons. The knowledge of the variables determining the allocation of mental resources may allow ergonomic interventions aimed at improving the safety of laparoscopic procedures. We assessed the subjective total workload (STW) during laparoscopic (LS) and open (OS) surgery.

Methods: Five Italian Surgical Centers participated. The NASA-TLX questionnaire was used to assess STW.

Results: 18 surgeons performed 65 procedures in the LS group and 39 in the OS group. A trend ($p = 0.095$) towards higher STW was observed in the OS group, with significantly higher temporal demand and frustration values. OS surgeons were older and more experienced and the mean duration of OS procedures was longer. In both groups, STW showed a double-peak distribution. Subgroup analysis showed higher mental and physical demand for laparoscopic procedures with higher STW.

Conclusions: NASA-TLX is a useful tool for assessing STW in the surgical setting. High and low STW subgroups can be identified in both OS and LS. Since many variables can potentially influence STW, larger studies are needed to identify them and to implement ergonomic measures for improvements.

Administrative Data and Inverse Occurrence of Cancer and Alzheimer's Disease in Elderly People I: A Methodological Approach to Control for Biases Due to Underdiagnosis

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Background: Lower incidence of cancer in persons with Alzheimer disease and vice-versa has been previously reported; this might be due to an under-diagnosis of the second disease after the occurrence of the first. Aim of this study was to estimate the unbiased co-occurrence of the two diseases in a population of about one million persons, using administrative health data (AHD).

Methods: In AHD we identified incident Cancer and AD cases over a period of five years. To control for under-diagnosis of the second disease three analyses were carried-out: 1. For times preceding or following the index diagnosis; 2. For surviving or not the follow-up period; 3. For different types and sites of cancer. Relative risks (RRs) of AD in persons with cancer and vice-versa, relative to the general population, were estimated as observed timed expected cases.

Results: The RRs of cancer in persons with AD and of AD in persons with cancer were both reduced. The inverse relationship of occurrence was independent from the temporal order of appearance of the diseases, from life-expectancy reduction and from different cancer types.

Conclusions: Administrative data represent a valid source for the conduction of cohort studies on the co-occurrence of diseases.

Extrapyramidal and Cognitive Signs in Amyotrophic Lateral Sclerosis: A Population-Based Case-Control Study

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Background: The association between Amyotrophic Lateral Sclerosis (ALS) and other neurodegenerative diseases is well-known. However, data are inconsistent about the possible association with Parkinson's disease (PD). Objective of this project was to assess the correlation between ALS, fronto-temporal dementia (FTD) and PD.

Methods: From May 2007 through August 2012 we investigated 146 patients with newly diagnosed ALS and 146 age and sex-matched controls. Each individual was screened for cardinal extrapyramidal signs (neurological examination) and cognitive dysfunction (Minimental State Examination and Frontal Assessment Battery, FAB).

Results: Rigidity was present in 8.2% of cases and 2.0% of controls ($p = 0.03$; adjusted Odds Ratio, adjOR 5.8; 95% confidence

interval, 95% CI 1.4–23.1). The corresponding percentages for bradykinesia and postural instability were 8.2 vs. 2.7% ($p = 0.07$; adjOR 4.3; 95% CI 1.2–15.5) and 2.7 vs. 9.6% ($p = 0.03$; adjOR 0.2; 95% CI 0.0–0.7). An abnormal FAB score (≤ 12) was recorded in 15.1 vs. 3.4% (adjOR 4.6; 95% CI 1.6–12.7). Tremor and abnormal FAB score were predicted by an older age at onset while an abnormal FAB score was associated with cramps and family history of dementia.

Conclusions: Our data confirm that newly diagnosed ALS carries a higher than expected risk of selected extrapyramidal disorders and FTD.

Traumatic Event and ALS: An European Case-Control Study

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Background: An Italian study on the association between amyotrophic lateral sclerosis (ALS) and trauma found that antecedent, repeated and severe trauma may be risk factors for ALS. These data required replication in other countries.

Methods: A case-control study was undertaken in Italy, France, England, Ireland, and Serbia. Cases were patients with newly diagnosed ALS from seven population-based registries. For each case, two controls were selected from the general practitioners' lists, matched for age, sex, and residency. Traumatic events occurred 5+ years before ALS onset were recorded with details on type, site, timing, severity, and complications. The risks were assessed as odds ratios (ORs) with 95% confidence intervals (CI), crude and adjusted for age, sex, education, interviewee (patient or surrogate), physical activity, BMI, smoking, alcohol, and coffee.

Results: 575 patients and 1150 controls were enrolled. One or more traumatic events were reported by 28.7% of cases and 27.83% (OR 1.10; 95% CI 0.87–1.39). The ORs was 1.34 (95% CI 1.04–1.72) for moderate traumatic events, 1.54 (95% CI 1.24–1.92) for traumatic events leading to disability and 2.94 (95% CI 1.25–6.92) for 2+ traumatic brain injury (TBI).

Conclusions: Moderate to severe traumatic events and repeated TBI are risk factors for ALS.

Hereditary Spastic Paraplegia in Sardinia: Epidemiology and Clinical-Genetic Characterization

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Background: Hereditary spastic paraplegias (HSP) are heterogeneous rare neurodegenerative disorders. We explored HSPs epidemiological, clinical and genetic variability among Sardinians, a population of peculiar ethnicity.

Methods: A population-based prevalence study was performed in north-western Sardinia. Multiple sources were used for case ascertainment. Familial and sporadic cases were diagnosed according to accepted criteria. Clinical data and pedigree information were recorded and blood samples drawn for genetic testing.

Results: On 31 December 2010, the total crude prevalence was 19.9 per 100,000 (95% CI: 18.4–21.4), 17.5 for autosomal dominant HSP, with 76% of prevalent cases presenting the same large SPAST deletion. In some areas, geographic isolation favoured the spread of a SPG4 kindred from few founders. Most of patients presented a mild disability as reported for another SPG4 family in southern Sardinia, with a small gene deletion. A 17-year-old boy from the inland presented the clinical features of Infantile Ascending Hereditary Spastic Paraplegia (IAHSP), carrying an ASL2 novel mutation.

Conclusion: HSP prevalence among Sardinians is high compared with other European populations. The deletion of SPG4 is the most represented mutation associated to an older age at onset, longer disease course and mild disability. Investigating the genes flanking SPG4 as disease modifying factors is worthwhile.

Reduced Duration of Breastfeeding Is Associated with a Higher Risk of MS in Both Italian and Norwegian Adult Males: The EnvIMS Study

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Background: Longer duration of breastfeeding is associated with a reduced risk of allergic and immune-mediated diseases including multiple sclerosis (MS). With a large multinational case-control study, we investigated the association between breastfeeding and MS risk in two distinct populations.

Methods: A questionnaire (EnvIMS-Q) eliciting information on feeding practices during the first year of life was administered to individuals with MS and frequency age and sex-matched controls from Italy and Norway. Two exposure categories were created: breastfeeding for at least 4 months (reference), no breastfeeding/breastfeeding for 3 months or less (reduced exposure). Logistic regression with odds ratio (ORs) and 95% confidence intervals (95% CIs), adjusting for covariates was used to assess the association.

Results: 547 cases and 1039 controls in Italy, and 737 cases and 1335 controls in Norway were included. A significant association of MS with 'reduced exposure' to breastfeeding was found in Italy (OR_{adj} = 1.37 (1.09, 1.73)), but not in Norway (OR_{adj} = 1.13 (0.91, 1.40)). For both countries significant associations were observed in men (OR_{Italy} 2.33 (1.50, 3.65), OR_{Norway} 2.11 (1.30, 3.44)).

Conclusion: Shorter duration of breastfeed was associated with an increased risk of MS in men in Italy and in Norway.

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Pregnancies Modify Disease Course of Multiple Sclerosis

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Background. Previous studies indicated that pregnancies modify short disease course of multiple sclerosis (MS), but effects on long term prognosis are inconsistent.

Methods: Using a structured face-to-face questionnaire we obtained information about year, number and characteristics of pregnancies in women with MS. These were matched with a clinical database to obtain the following characteristics: number and duration of relapses before or after pregnancies, the proportion of relapses with complete or incomplete recovery. We compared relapse rate (RR), duration of relapses, proportion of relapses with complete recovery between women who had pregnancies before MS onset and women who didn't.

Results: Age at onset was earlier in nulliparous women with MS (24.7 years vs. 27.3 in women with pregnancies). RR was significantly lower in women with pregnancies before onset compared to nulliparous (0.4 vs. 4.1; $p < 0.05$). Women who became pregnant before MS onset had also a significantly higher proportion of relapses with complete recover compared to the others (2.9 vs. 1; $p < 0.05$).

Conclusion: Present study suggests a long lasting protective role of pregnancies on MS course and supports the observation that women with MS do not modify their propensity to have pregnancies even after having received the diagnosis.

Adhesion to SITS-WATCH: Door-to-Needle Time in a Single Centre Before and After Implementation of a Rapid Response Treatment Protocol for Patients with Acute Onset Stroke

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Background: we aimed to compare the door-to-needle time (DNT) in patients presenting with acute onset ischemic stroke treated with IV-tPA before and after the implementation of an in-hospital rapid response treatment protocol.

Methods: we conducted a retrospective analysis of all patients (n = 181) admitted to the Rivoli degli Infermi Hospital for acute ischemic stroke and treated with IV-tPA between April 2005 and August 2014. From January 2013 we reorganized the ER management of acute stroke treatment in order to speed brain CT and

laboratory results and clearly identify places and operators for IV-tPA administration in ER.

Results: From April 2005 to December 2012 we performed 116 IV-tPA with a mean DNT of 76 min (95% CI: 71–87). From January 2013 to August 2014 we treated 65 pts with a mean DNT of 54 min (48–59); $p < 0.0001$. After the introduction of the new treatment protocol, the number of patients treated increased, and case fatality ratio at 3 months remained stable (17% for the period 2005–2012 vs 15% in 2013–2014, $p = ns$).

Conclusions: We were able to significantly reduce the mean DNT by implementation of an in-hospital rapid response treatment protocol in our Centre.

The Epidemiology of Huntington's Disease in Modena and Reggio Emilia

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Background: Huntington's disease (HD) is a genetic progressive neurodegenerative disease with a worldwide prevalence of 5–10/100,000 residents and a progressive course. In Italy a lower prevalence of HD was found (1.9–4.8/100,000). This study aimed to calculate the prevalence of HD in the districts of Modena and Reggio Emilia on the 1st of July 2013 and the average incidence between 2003 and 2012. The phenotype at onset and its correlation with the genetic background have been also evaluated.

Methods: We examined the out-patient and hospital charts from the health care facilities of Modena and Reggio Emilia of patients diagnosed with HD.

Results: We found a prevalence of 2.5/100,000 residents and an average annual incidence of 0.19/100,000 residents. The disease started with choreoathetosis in most cases. In addition, in 26% of patients HD presented with choreoathetosis in the cranial and oro-mandibular region.

Conclusions: These results confirm the findings of studies carried out in other Italian areas. Clinical data also confirm the findings available in published reports.

Low Level of Education Is Associated with Increased Risk of Multiple Sclerosis in Italy: The EnvIMS Study

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Background: A higher risk of MS among persons with a low level of education has been recently reported. We investigated this association also in Italy and whether it reflected the effect of smoking and other factors related to lower levels of education.

Methods: Within the case-control study on Environmental risk factor In MS (EnvIMS), 691 MS patients and 1290 population-based controls from Sardinia and the province of Ferrara, Italy, reported educational level and past exposure to putative environmental risk factors including smoking, infectious mononucleosis, vitamin D-related diet, sun exposure and body size.

Results: We found a significantly decreasing MS-risk along with increasing educational level ($p = 0.01$) with an OR of 1.64 comparing those with the lowest to highest level of education. This association was stronger in Ferrara compared to Sardinia and was only moderately reduced after adjusting for known risk factors.

Discussion: The finding of an inverse association between level of education and MS risk also in Italy suggest that factors related to lower social class other than smoking and vitamin D related factors are associated with MS risk.

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Incidence and Time Trends of Brain Proteinopathies in Olmsted County, Minnesota Over Thirty Years

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Background: We investigated the incidence of proteinopathies from 1991 to 2005 and the time trends of parkinsonism and Parkinson disease (PD) over a 30-year period from 1976 to 2005.

Methods: We used the medical records-linkage system of the Rochester Epidemiology Project to identify all incident cases of parkinsonism in Olmsted County, MN, from 1991 to 2005 and we investigated the incidence over 3 decades: 1976–1985, 1986–1995, and 1996–2005. We used Poisson rate regression to test for trends.

Results: Among 542 incident cases of parkinsonism from 1991 to 2005, 409 (75.5%) were classified as proteinopathies. 264 had Parkinson's disease (48.7% of all cases). The incidence rate (per 100,000 person-years) of synucleinopathies was 21.0 overall and increased steeply with age. The overall age-adjusted incidence of parkinsonism in men increased from 38.9 in 1976–1985 to 55.9 in 1996–2005 (trend p -value = 0.0002). The age-adjusted incidence of PD in men increased from 18.2 in 1976–1985 to 30.4 in 1996–2005 (trend p -value = 0.0005). By contrast, the overall age-adjusted incidence of parkinsonism and PD in women did not change.

Conclusions: Our study suggests that the incidence of parkinsonism and PD are increasing over time in Olmsted County from 1976 to 2005 particularly in older men.

Atrial Fibrillation: A Rising Etiology of Cardioembolic Stroke. Report from a First Level Stroke Unit

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Background: Cerebrovascular disease is the second commonest cause of death after ischemic heart disease and it is a leading cause of disability worldwide. Atrial fibrillation (AF) is the most common cardiac arrhythmia associated with a fivefold increased risk of stroke.

Methods: We collected medical data of all patients undergoing thrombolysis from July 2010 to June 2014 in our Stroke Unit (SU) and we have made a statistical analysis of them.

Results: We treated 87 patients (male 56; mean age 68.7 y). The mean time of door-to-needle treatment was 92 minutes. A reduction of the NIHSS score after thrombolysis occurred in 78% ($p < 0.0001$). The etiology of stroke was principally cardioembolic, half

of cases presenting paroxysmal AF. Anterior circulation syndrome predominated (68%). The mean time of recovery in SU was 6.2 ± 4.7 days. 15 patients (17.2%) went home directly from SU and other 56 after transfer to the neurology department.

Conclusions: AF is the is the commonest sustained cardiac arrhythmia and the most important cause of cardioembolic stroke. We have registered a higher prevalence of cerebral infarct due to AF in our population than in other reports (Caplan LR, et al. 1983; Arboix A, et al. 2014). In most cases, recurrence of cardioembolism can be prevented by oral anticoagulants (secondary prevention). This fact deserves attention as oral anticoagulants with a better risk:benefit ratio are now available.

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Online Multidisciplinary Record to improve Amyotrophic Lateral Sclerosis (ALS) Care: The Umbria Region ALS Integrated System

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Background: Challenges in amyotrophic lateral sclerosis (ALS) clinical management include the optimization of interdisciplinary approach during disease progression. The prompt collection and easy availability of data should improve both communication between involved physicians and information for patients.

Methods: A web application for the management of ALS patients was developed by the Umbria Regional Centre which plays a central role in the network organization of involved health districts. The online multidisciplinary record comprises dedicated webpages for neurological, pneumological, otolaryngological, nutritional/gastroenterological, psychological practice, palliative care, social support, rehabilitation systems, tracheostomy/gastrostomy tube placement, and finally anticipated dispositions.

Results: The application is in use since 2011 and can be accessed for data entry or consultation by involved specialists; currently 91 patients have been recorded. The extraction of subgroups with specific demographic (i.e. age, sex), clinical (i.e. patients with gastrostomy, drug intakes) and social features was implemented. The monitoring of specific parameters (i.e. ALSFRS-R score) is available for each patient.

Conclusions: The web application allows integrating crucial information in a real-time manner to improve patient's care and to record all ALS patients in a regional database. The authors encourage its use for multidisciplinary follow-up evaluations, outcome measures export and health care costs estimation.

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Prevalence of Different Types of Dementia in a Population Based Study in Southern Italy: The GreatAge Study

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Background: Prevalence of dementia has been studied mainly in a clinical setting. Most population-based studies have been conducted outside Italy.

Methods: Subjects over 65 years were recruited in Castellana Grotte, Southern Italy as the fourth wave of a cohort study on cancer and nutrition (MICOL), started in 1986. All subjects invited to a clinical center underwent a neurological and neuropsychological examination as part of multidisciplinary assessment. Dementia diagnosis was made according to Diagnostic and Statistical Manual of Mental Disorders–IVR edition. Dementia subtypes were diagnosed according to current international diagnostic criteria. The Clinical Dementia Rating Scale was used to define dementia severity.

Results: We enrolled 514 subjects (312 males and 202 females; mean age 72.84 ± 6.12 years; mean education level 6.59 ± 3.63 years). Dementia was diagnosed in twenty-five patients (5%) (17 mild, 6 moderate, and 2 severe). The most frequent subtype of dementia was Alzheimer's Disease (17/25, 68%), followed by Vascular Dementia (3/25, 12%), frontotemporal dementia (2/25, 8%), Parkinson's Disease with Dementia (2/25, 8%), and Lewy Body Dementia (1/25; 4%).

Conclusions: These preliminary results showed a prevalence of dementia lower than most published studies. Possible explanations will be discussed.

Questioning the Clinical Utility of Amyloid Pet in the Diagnostic Management of Subjects with Cognitive Impairment

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Background: Two amyloid ligands, florbetapir (18F) and flutemetamol (18F), have been approved by both the Food and Drug Administration (FDA) and the European Medicines Agency (EMA). The objective of this commentary is to discuss data from the Summary of Product Characteristics (SPC) of Amyvid (florbetapir) and the conclusions based on that data.

Methods: All data reported in the SPC were gathered along with sources from which they were taken. Reported values of sensitivity and specificity were checked for consistency. Appropriateness of the methodology used was assessed.

Results: Diagnostic parameters are appropriately calculated when estimating the ability of PET to correctly identify the presence or the absence of amyloid plaques. Reasoning in terms of diagnostic accuracy seems instead inappropriate when analyzing the association between PET and a diagnosis of MCI or AD, and the ability of the test to predict conversion from MCI to AD.

Conclusions: No definite evidence links the presence of amyloid plaques to a diagnosis of AD or MCI, nor to a inevitable and faster cognitive decline. Though PET is highly accurate in identifying the presence or the absence of amyloid plaques, to whom and to which purpose could it be prescribed remains unclear.

Genetic Susceptibility Markers Have No Effect on Multiple Sclerosis Disability Outcomes

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Background: We aimed to analyze the association of genetic markers on the development of disability in an Italian cohort of 307 multiple sclerosis (MS) patients.

Methods: Patients were enrolled from January 2001 in two MS Centers and followed till the occurrence of an expanded disability status score (EDSS) of 3 maintained for at least six months, or June 30, 2014, whichever came first (mean follow-up: 11.1 ± 6.9 years). We genotyped all the patients for 3 HLA loci (*DRB1*15*, *A*02*, *DRB1*03*) and a subset of 124 patients for the 107 non-HLA SNPs associated with MS susceptibility (International Multiple Sclerosis

Genetic Consortium). A weighted Genetic Risk Score (wGRS) was calculated.

Results: The cumulative probability of reaching EDSS 3 ten years after onset was similar ($p = ns$) for the three tertiles of the wGRS: 23.0% (± 0.08) for the lowest, 19.8 (± 0.05) for the intermediate, and 20.3 (± 0.08) for the highest. None of the single HLA markers influenced the probability of attaining EDSS 3.

Conclusions: The 110 established genetic variants for susceptibility to MS have probably little influence in the development of disability after 10 years of disease.

How to Settle Disagreement in Defining Diagnostic Criteria for a Rare Neurologic Condition: The Example of the International Consensus Conference on Nocturnal Frontal Lobe Epilepsy

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Background: A consensus conference (CC) is a systematic method by which a community comes to an agreement about a controversial topic, facing the scarcity of evidence. Nocturnal Frontal Lobe Epilepsy (NFLE) is a rare condition with unresolved core features.

Methods: Method according to the Italian Handbook for CC (2009). Promoter: IRCCS Neuroscience of Bologna. Four entities: Scientific committee planned the project and questions; Technical committee performed the systematic review (SR); Workgroups of experts provided answers on clinical history, neurophysiology, etio-pathogenesis; Consensus panel chaired the CC and provided statements. Four phases: assignment; scoping; assessment; CC event.

Results: Activities: from November 2013 to September 2014. After the nomination (assignment) of participants (from three continents, representing the perspectives of epilepsy, sleep, epidemiology), questions were identified (scoping). Workgroups appraised the state-of-knowledge of NFLE produced by the SR (assessment). CC event was held over 2 days: Workgroups discussed the answers; the Consensus panel – after agreement – drafted statements for the new diagnostic criteria.

Conclusions: CC relies on a distinction between those who provide the evidence (experts) and those who draw the statements (panel). The CC model could be a valuable tool for the construction of explicit conclusions in controversial topics such as rare disorders.

Personality Traits Are Predictors for Health Related Quality of Life Outcomes in Persons with Multiple Sclerosis

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Background: To date, few studies are reported on the possible role of personality traits as predictors of health-related quality of life (HRQoL) in persons with multiple sclerosis (PwMS). We investigated the role of extraversion, neuroticism and psychoticism as possible predictors of HRQoL in a large cohort of PwMS.

Methods: 250 PwMS (Poser criteria) were consecutively recruited at our MS center. PwMS' self-perceived health status was assessed with the 36-Item Short Form Health Survey (SF-36). Personality traits were assessed by administering the Eysenck Personality Questionnaire (EPQ-R, Italian version). Changes in HRQoL according to personality traits were investigated by means of univariate analysis of co-variance (ANCOVA) and general linear model procedure.

Results: 195 out of 250 MS patients (F:M = 2.75), aged 41.7 ± 10.2 years were included in the analysis, after screening for major intellectual deficits and anxiety status. SF-36 MCS and PCS variance was largely explained by extraversion ($p < 0.0001$), neuroticism ($p < 0.0001$), psychosis ($p < 0.0001$).

Conclusions: Taken together, our data clearly indicate that the personality traits of PwMS influence self-perceived HRQoL. An assessment of personality in the context of a psychological approach to PwMS should be part of routine clinical assessment.

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Onabotulinum Toxin-A for Treatment of Chronic Migraine: Real-Life Data in 36 Patients from San Giovanni Rotondo

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Background: Chronic migraine is a underdiagnosed neurological disorder affecting approximately 2% of the population and is associated with disability and poor quality of life. The two Phase III REsearch Evaluating Migraine Prophylaxis Therapy (PREEMPT) clinical trials showed that onabotulinumtoxinA is a safe, well-tolerated, and effective prophylactic therapy for patients with chronic migraine. In Italy Botox® (onabotulinumtoxinA) was licensed for the *treatment of chronic migraine* in February 2013, and there are few real-life data of its use.

Method: 36 adults with chronic migraine were injected with Botox® between April 2013 and July 2014. The protocol of the study required the injection of 155 units of botulinum toxin-A in 31 fixed sites at a fixed-dose of five units in each muscle. At the investigator's discretion, up to 40 U of additional toxin could be administered. Headache data were collected using patient diaries and records were reviewed for migraine days, headache hours, headache-free days, analgesic medication use, triptan use and nausea.

Results: OnabotulinumtoxinA significantly reduced the use of analgesic medication and the number of headache hours. It also significantly increased the number of headache free days.

Conclusion: OnabotulinumtoxinA is a useful adjunct to current treatment options in adults with chronic migraine.

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