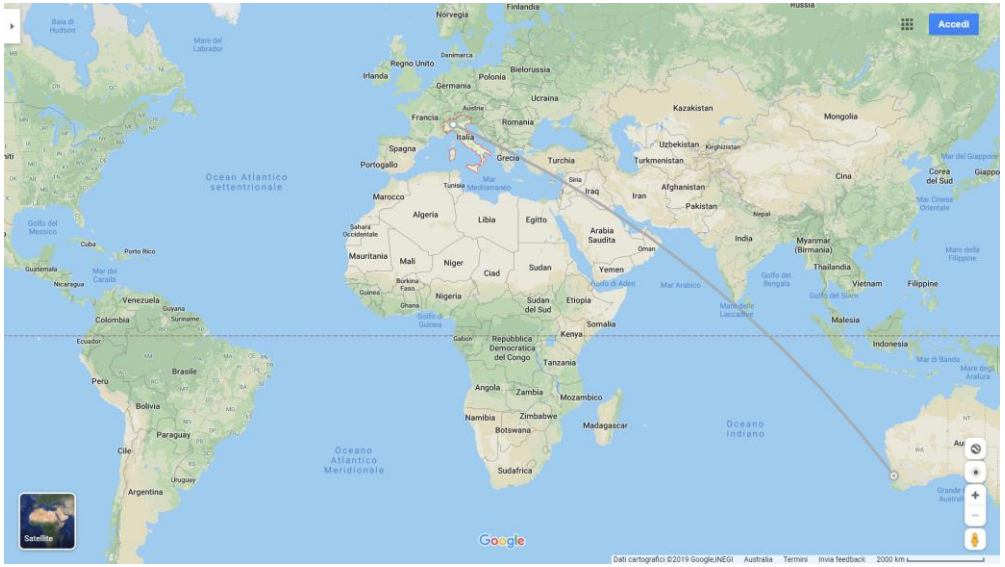
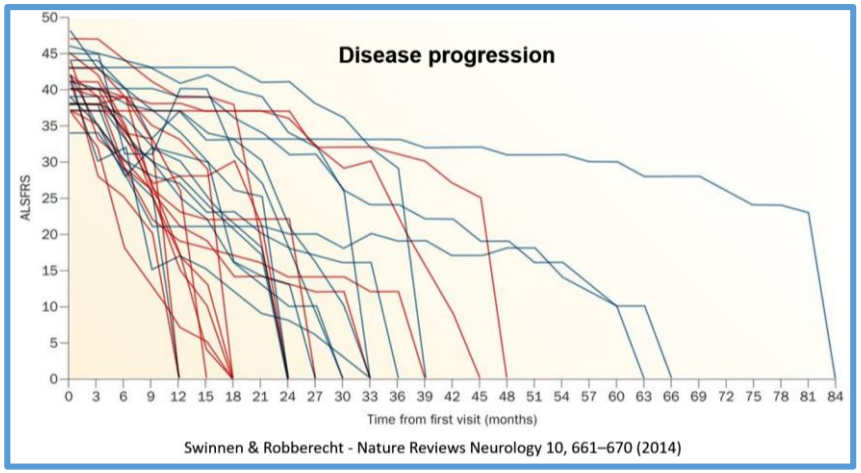
The Italian ALS Patient-driven registry and The ALS Biobank: two new tools to promote and stimulate the research

Christian Lunetta

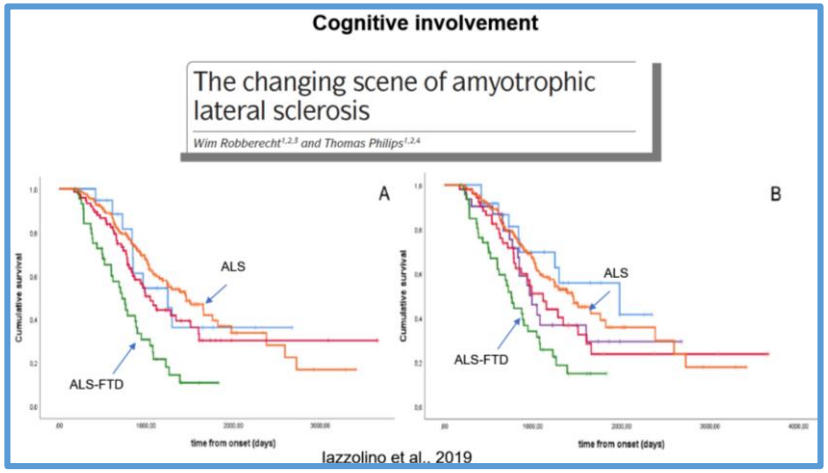


Alliance Meeting December 1 – 2, 2019 Perth, Western Australia

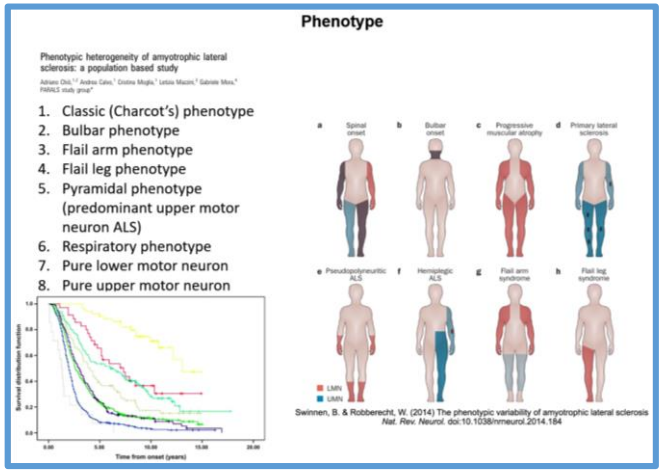
ALS is rare and clinically heterogeneous disease

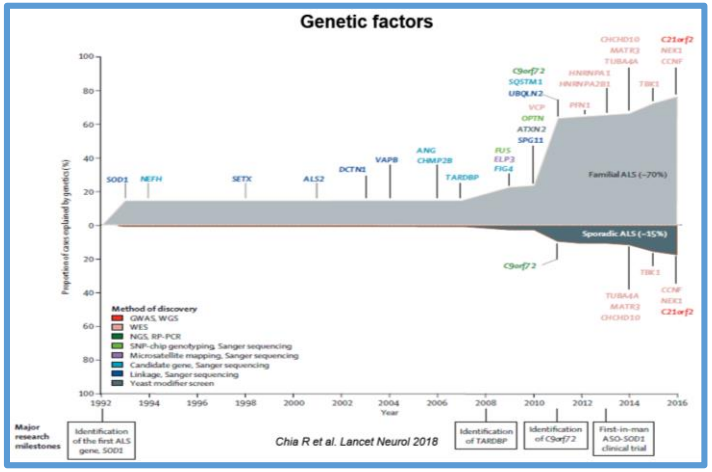


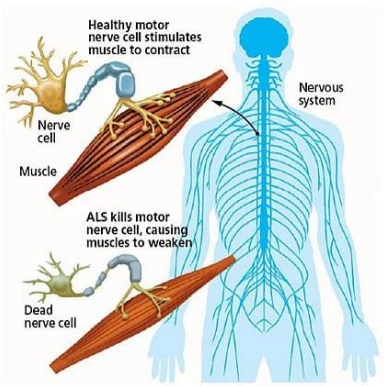
Swinnen & Robberecht - Nature Reviews Neurology 10, 661–670 (2014)



Iazzolino et al., 2019







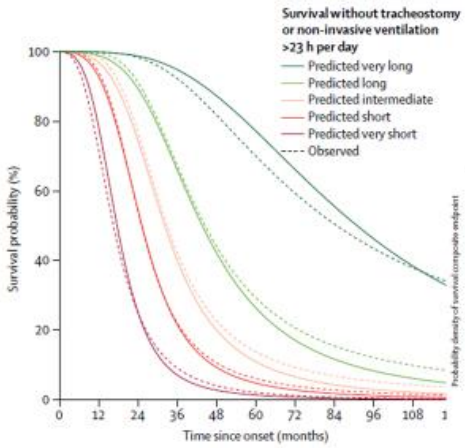
ALS is rare and clinically heterogeneous disease, and to better understand the demographic characteristics of people living with ALS (PALS), the natural history of ALS across all phenotypes, and disease management in the real-world setting, requires large-scale data collection and harmonization.

Lancet Neurol 2018; 17: 423–33

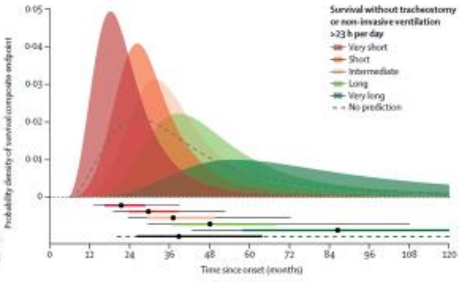
Prognosis for patients with amyotrophic lateral sclerosis: development and validation of a personalised prediction model

Eight of the 16 candidate predictors were selected for the multivariable prediction model

Age at onset (years)
Diagnostic delay (months)
Progression rate (points per month)
Forced vital capacity (%)
Bulbar onset
Definite ALS¶
Frontotemporal dementia
C9orf72 repeat expansion



The model identified five groups with distinct survival times (median in months) from symptom onset:
- Very short 17.7;
- Short 16.5,
- Intermediate 32.2;
- Long 43.7;
- Very long 91.0.



11 475 patients
14 Centers

Large-scale data collection and harmonization can be done via several mechanisms, including:

- population-based disease registries,
- voluntary direct reporting by patients (patient-driven registry),
- merged databases from individual clinical research efforts,
- clinic-based data repositories.

In Italy we have only 4 Regional population-based disease registries:

- Piemonte – Val d'Aosta
- Puglia
- Emilia-Romagna
- Liguria

Large-scale data collection and harmonization can be done via several mechanisms, including:

- population-based disease registries,
- voluntary direct reporting by patients (patient-driven registry),
- merged databases from individual clinical research efforts,
- clinic-based data repositories.

Susan Desmond-Hellmann is the Chancellor of the University of California, San Francisco, San Francisco, CA 94143, USA.

Citation: S. Desmond-Hellmann, Toward Precision Medicine: A New Social Contract? *Sci. Transl. Med.* **4**, 127ed3 (2012).

10.1126/scitranslmed.3003473

EDITORIAL

POLICY

Toward Precision Medicine: A New Social Contract?

EARLIER THIS YEAR, ILLUMINA INC. AND LIFE TECHNOLOGIES INC. EACH ANNOUNCED new products that can sequence a genome for $1,000 in a single day (*1*); approximately 3 million times cheaper than the cost during the Human Genome Project back in the early part of the last decade. Furthermore, cloud-based, big-data software companies are capable of using whole- and partial-genome sequencing to automate and operationalize diagnostics in real-life situations with patients. But no one believes that less expensive data and more analyses are in themselves enough to accelerate the path to disease cures. In fact, science writer Nicholas Wade asserted in the 12 June 2010 issue of the New York Times that, a decade after completion of the first draft of the human genome sequence, too little clinical benefit has been realized (*2*). Many have subsequently defended the human genome project's benefits; but it remains reasonable to ask why, given the explosion of scientific knowledge in the last decade, haven't we seen greater gains in health outcomes?

A new National Research Council report (3) from the U.S. National Academies (http://

Susan Desmond-Hellmann
Chancellor of the
University of California

I believe that the most important requirement for the new knowledge network envisaged by the Precision Medicine report is that it be driven by patients. Indeed, it is patients who uniquely understand the potential value of a social contract in which patients both contribute personal clinical data and benefit from the knowledge gained through the collaboration. Patients are also in the best position to demand the sharing of both data and professional credit that will be necessary to fully capture the value of this new collaborative approach to acquiring, synthesizing, and widely disseminating biomedical knowledge

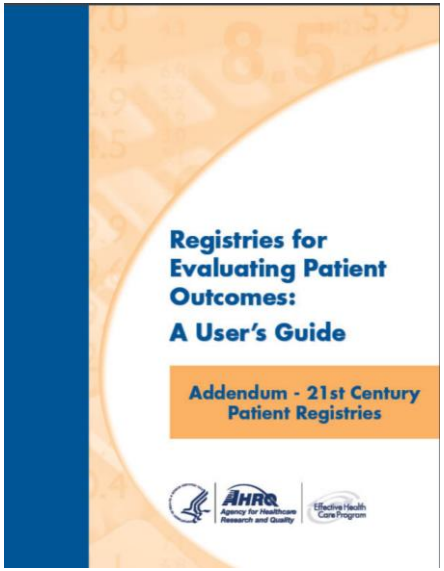
Napier *et al. Orphanet Journal of Rare Diseases* (2017) 12:134
DOI 10.1186/s13023-017-0686-1

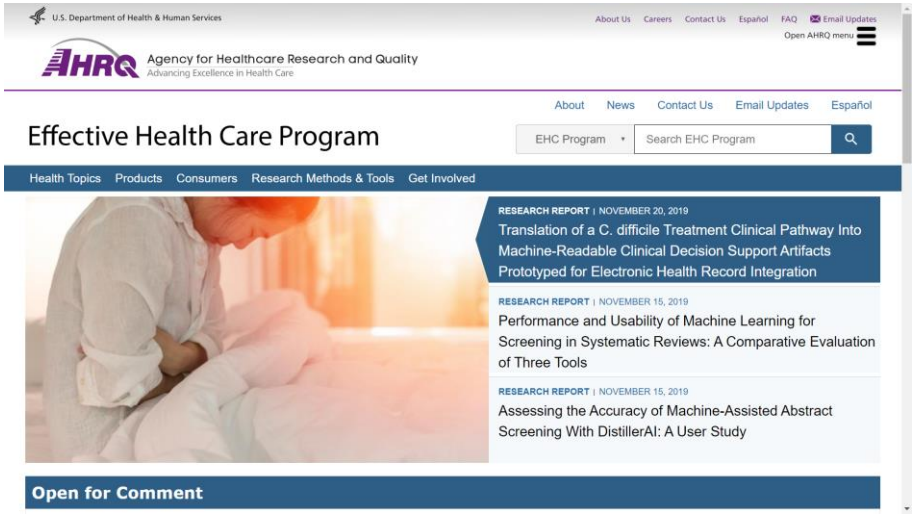
Orphanet Journal of Rare Diseases

LETTER TO THE EDITOR Open Access

A web-based, patient driven registry for Angelman syndrome: the global Angelman syndrome registry

Kathryn R. Napier[1], Megan Tones[2], Chloe Simons[3], Helen Heussler[4], Adam A. Hunter[1], Meagan Cross[3] and Matthew I. Bellgard[1*]





The concepts of **patient-centered care** and **patient-centered research** have moved to the forefront of health care and research in recent years

The definition of **patient-centered care** as "providing care that is respectful of and responsive to individual patient preferences, needs, and values, and ensuring that patient values guide all clinical decisions"

The definition of **patient-centered outcome research** as "research that addresses the questions and concerns most relevant to patients."

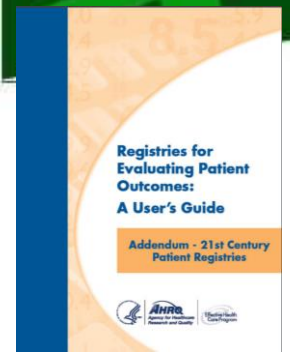


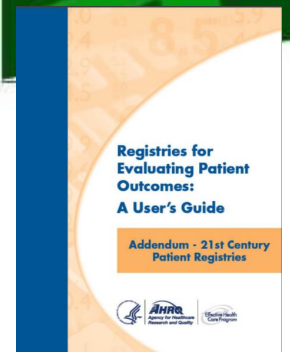
Table 1-1. Goals and benefits of patient-centeredness in research and medical care

THEME	GOALS
Funding	Research funding is directed optimally to address questions that are of high priority and relevance to patients
Research design	To align research questions with evidence gaps and patient needs as well as enhance research efficiency
Availability of evidence and dissemination	Dissemination of research findings to health care providers and patients is timely and transparent, and communicated in a manner that is clear and understandable to patients
Informed decision-making	Patients have the necessary information to make informed decisions about the health care choices available to them, linked to health outcomes that are important to them
Desired benefits	• Improvement in health outcomes that are most meaningful to patients and clinicians • Increased satisfaction of patients and health care providers with medical care

Patient-centered care and patient-driven clinical research is intended to result in two primary outcomes:

(1) increased satisfaction of patients and health care providers with medical care;

(2) improvement in health outcomes that are most meaningful to patients and clinicians



Patient registry is "an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes."

In comparison to other research designs, patient registries offer some unique features that may be particularly useful for patient-centered outcomes research (PCOR).

Patient-Powered Research Networks →

Goals for the PPRNs are similar to those for many disease registries, with each network being focused on a specific condition and/or community of interest with an objective of creating a standard database that can be used to address future patient-driven research questions.

A hallmark of the PPRNs is to include patients as partners in the governance structure of the network and to collect PROs relevant to the community they serve to support patient-prioritized PCOR questions.

REGISTRO SLA

ITalian ALS Registry: a pilot study to assess the feasibility of a web-based, patient driven registry for Italian people with Amyotrophic Lateral Sclerosis

Alliance Meeting December 1 – 2, 2019 Perth, Western Australia

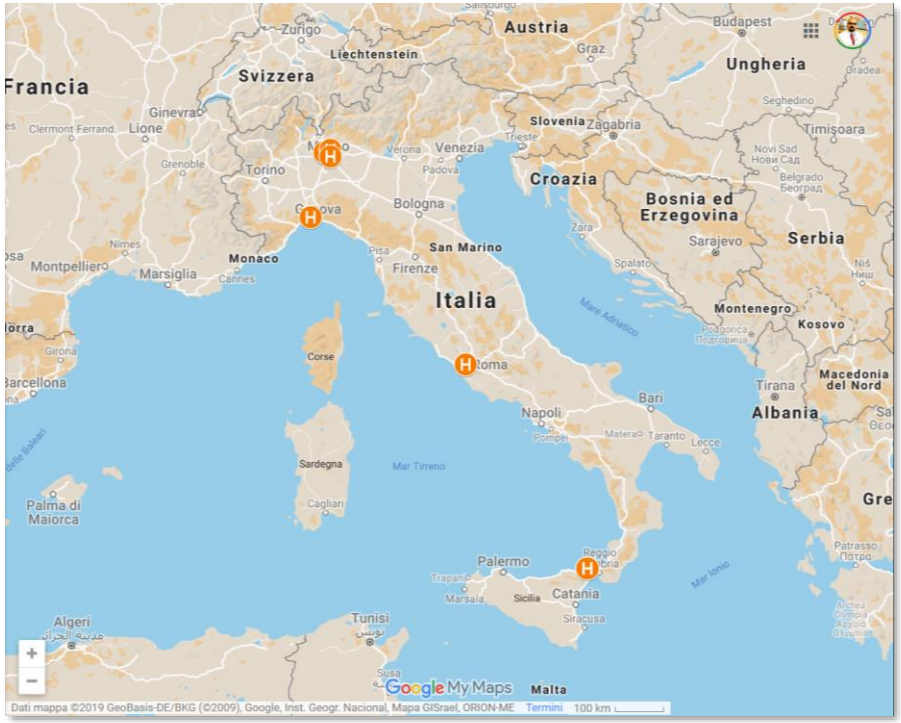
Secondary aims

1. Collect information on the distribution of ALS patients in Italy;
2. Collect data on the clinical, genetic and demographic characteristics of patients diagnosed with ALS, allowing greater knowledge of the disease and constant monitoring of any changes;
3. Contribute to the design of clinical trials and help identify suitable patients for clinical trials;
4. Collect data on the assistance received for the implementation of care standards;
5. Align data collection with a repository of biological material from ALS patients;
6. Encourage the networking of Italian clinical reference centers for ALS

REGISTRO SLA

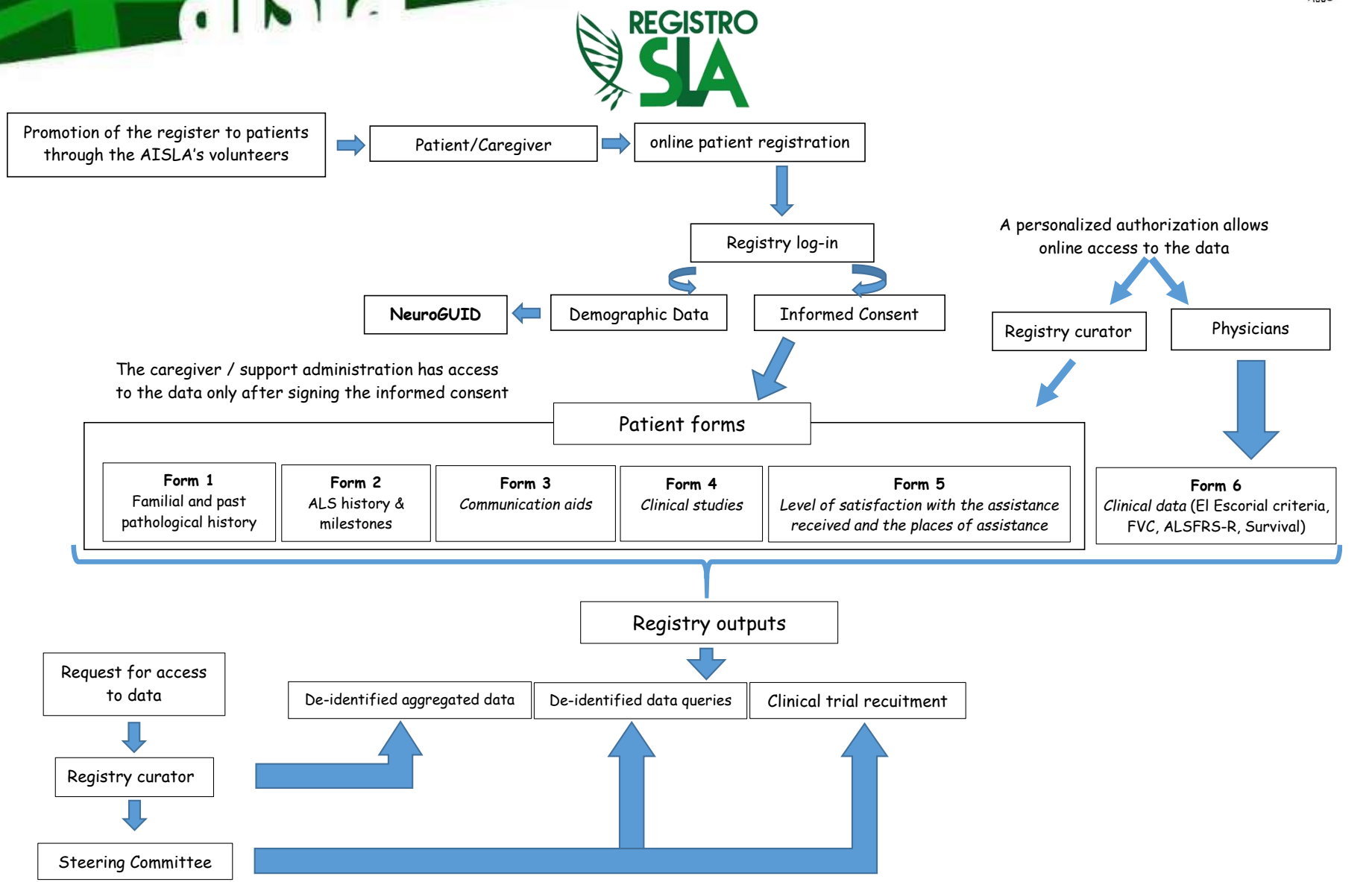
Participants

- **Promoting and supporting partner**: AISLA Association
- **Coordinating Center**: NEMO Clinical Center Milano (PI: Christian Lunetta)
- **Participating Centers**:
  - NEMO Clinical Center Arenzano (PI: Fabrizio Rao)
  - NEMO Clinical Center Roma (PI: Mario Sabatelli)
  - NEMO Clinical Center Messina (PI: Gianluca Vita)
  - S. Gerardo Hospital, Milano (PI: Lucio Tremolizzo)
  - S. Raffaele Hospital, Milano (PI: Nilo Riva)
- **Technical supporting partner**: Associazione del Registro Italiano dei pazienti con Malattie Neuromuscolari (PI: Anna Ambrosini)



Referral general population: 22,5 million inhabitants (1/3 of Italian population)
Referral ALS population: 1.600 – 2.100 patients

REGISTRO SLA


REGISTRO SLA
Promotion of the register to patients through the AISLA's volunteers
Patient/Caregiver
online patient registration
Registry log-in
A personalized authorization allows online access to the data
NeuroGUID
Demographic Data
Informed Consent
Registry curator
Physicians
The caregiver / support administration has access to the data only after signing the informed consent
Patient forms
Form 1
Familial and past pathological history
Form 2
ALS history & milestones
Form 3
Communication aids
Form 4
Clinical studies
Form 5
Level of satisfaction with the assistance received and the places of assistance
Form 6
Clinical data (El Escorial criteria, FVC, ALSFRS-R, Survival)
Registry outputs
Request for access to data
Registry curator
Steering Committee
De-identified aggregated data
De-identified data queries
Clinical trial recuitment

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

MASSACHUSETTS GENERAL HOSPITAL

Neurological Global Unique Identifier (NeuroGUID™)

What is NeuroGUID™

The Neurological Global Unique Identifier (NeuroGUID™) is a universal patient identifier that allows researchers in Neurological and other Central Nervous System diseases to share data specific to a study participant without exposing personally identifiable information (PII). It also enables matching participants across studies and research data repositories. In other words, NeuroGUID™:

- Allows aggregation of data from the same patient from multiple studies, regardless of where and when that data was collected
- Prevents a single patient from being created multiple times in the same research database, in case she/he participates in a study at different sites or in multiple studies at the same time
- Enables a researcher to combine patient information with data originating from other sources.

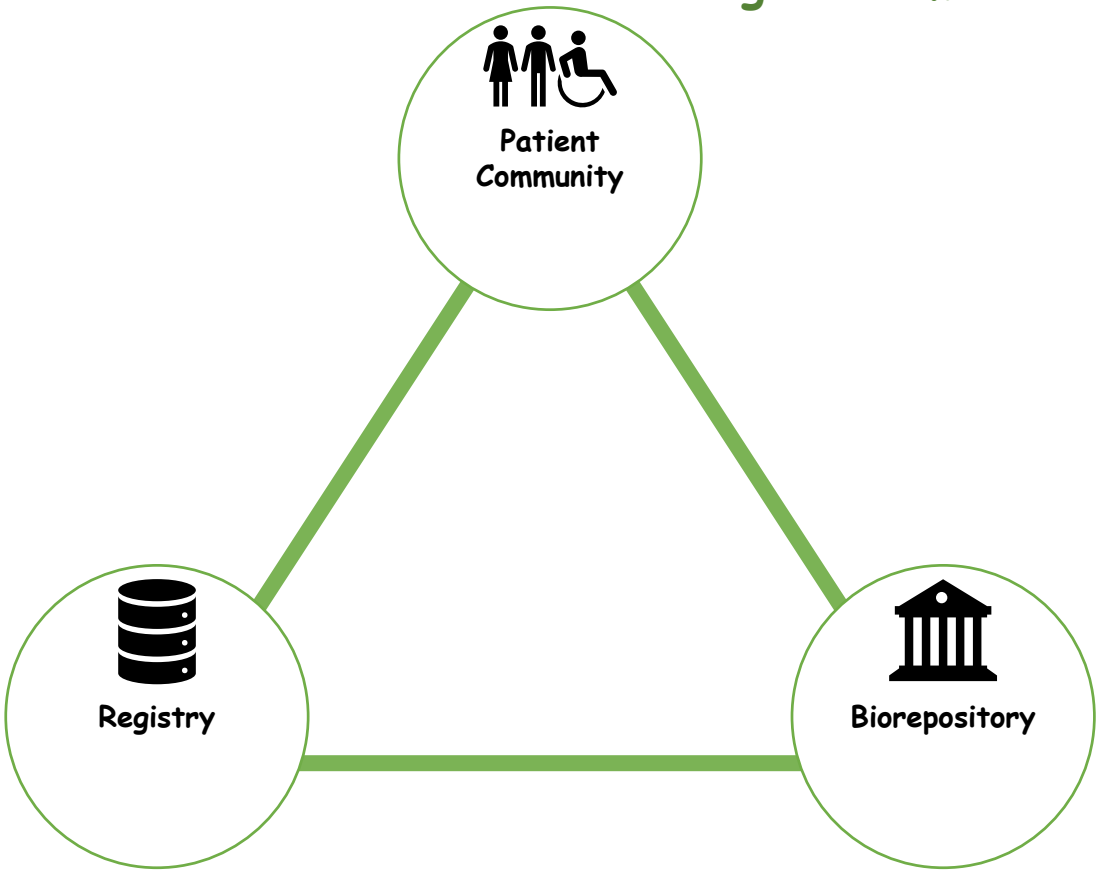
What information is required to create a NeuroGUID™

The following information is required to create a NeuroGUID™:

- Complete legal given first, middle and last names of patient at birth
- Date of birth
- Physical sex of patient at birth
- Name of city/municipality in which patient was born
- Country of birth

http://www.NeuroGUID.org

According to the principles of **patient-centered care** and **patient-centered research** we have built **an integrated model**



Main Aims

- ✓ To encourage research for the identification of genetic mutations and other causes of disease
- ✓ To support the collection of biological material coming from ALS people with genomic features useful for understanding the genetic basis of the disease
- ✓ To standardize the quality of biological material available
- ✓ To ensure the cryopreservation and availability for a long time of biological material suitable for the needs of scientific research according to the evolution of knowledge about the disease

BIOGem
BIOREP GEMELLI BIOBANK

aisla ONLUS
ASSOCIAZIONE ITALIANA
SCLEROSI LATERALE AMIOTROFICA

Gemelli
Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

il Fatto Quotidiano.it

Sla, nasce la prima biobanca nazionale: "Aperta a tutti, darà impulso alla ricerca"

È stata inaugurata dal presidente Conte al Policlinico Gemelli di Roma. Al suo interno, Dna, plasma e colture di cellule verranno catalogati in forma anonima e messi a disposizione di tutti i ricercatori italiani e del resto del mondo

di Chiara Daina | 21 Giugno 2019

INTERNATIONAL ALLIANCE OF ALS/MND ASSOCIATIONS

affaritaliani.it
Il primo quotidiano digitale, dal 1996

M5S Conte Salvini Di Maio

ATTIVA LE NOTIFICHE

FONDATORE E DIRETTORE: ANGELO MARIA PERRINO

Con il supporto non condizionato di Shire Italia Spa (ora parte di Takeda)

Home > Salute > Malattie rare >Giuseppe Conte inaugura a Roma la prima Biobanca nazionale sulla SLA

MALATTIE RARE

Lunedì, 17 giugno 2019 - 20:13:00

Giuseppe Conte inaugura a Roma la prima Biobanca nazionale sulla SLA

Il Presidente del Consiglio partecipa all'evento che coincide con la Giornata Mondiale sulla SLA (Sclerosi Laterale Amiotrofica), celebrata il 21 giugno

Foto LaPresse

di Lorenzo Zacchetti

Giovedì 20 giugno il Presidente del Consiglio Giuseppe Conte presenzierà all'inaugurazione della prima Biobanca nazionale sulla SLA (Sclerosi Laterale Amiotrofica).

Situata presso il Policlinico Universitario A. Gemelli IRCCS, è la prima Biobanca in Italia completamente dedicata alla ricerca scientifica su questa patologia e accessibile a tutti i ricercatori del mondo.

La Biobanca è stata realizzata da AISLA.

la Repubblica

20 giugno 2019

Medicina E Ricerca

Inaugurata a Roma la prima biobanca nazionale sulla Sla

Il premier Conte all'inaugurazione della Biobanca sulla Sla al Policlinico universitario A.Gemelli (ansa)

BIO BANCA NAZIONALE SLA

Factors of success and innovation

- ✓ It will collect biological specimens from a nationally representative sample of PALS, in particular that is not tied to a specific Center.
- ✓ It will help to collect sample from peripheral Centers that do not have facilities for a biobank
- ✓ It will be an open access biobank where researchers will be able to gain samples from ALS patients.
- ✓ It will be open to all researchers
- ✓ Together with ALS registry, it will help to create a network of neurologist and researchers across the country

BIO BANCA NAZIONALE SLA

What types of samples will be available?

- ✓ Blood
- ✓ Serum
- ✓ Plasma
- ✓ DNA
- ✓ RNA
- ✓ PBMCs
- ✓ Urine
- ✓ CSF
- ✓ Muscle
- ✓ Skin
- ✓ Human primary cells derived from PBMC of PALS with specific genetic background

BIO BANCA NAZIONALE SLA

BIO BANCA NAZIONALE SLA

to be continued...