A PARADIGM SHIFT IN THE EARLY DIAGNOSIS AND THERAPY OF DEMENTIA. THE ITALIAN APPROACH TO THE NEW SCENARIO.

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THE CHALLENGE OF ALZHEIMER'S DISEASE IN ITALY

EPIDEMIOLOGY, SOCIO-ECONOMIC IMPACT AND URGENCY OF INNOVATION

- **Growing epidemiology:** In Italy it is estimated that over **1 million people** currently suffer from dementia, 60%of whom with a diagnosis of AD. **Demographic aging** will lead to a **doubling of cases by 2050.**
- **Socio-economic impact**: The total annual cost of dementia in Italy exceeds **15 billion euros**, with more than **70% of the costs** provided by families (**informal care**).
- **Complex care challenge:** The disease requires **multidimensional care**, involving early diagnosis, pharmacological and non-pharmacological treatments, caregiver support and integrated **territorial services**.

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DEMENTIA CARE IN ITALY

PLEASE REFER FOR MORE INFORMATION TO: WWW.ALZINT.ORG/WHAT-WE-DO/POLICY/DEMENTIA-PLANS/

FROM **1996**:
REGIONAL LEVEL INITIATIVES

→ Initial Funding for specialized training of health assistance operators

FROM **2000**:
"CHRONOS" PROJECT

→ **500 diagnostic center (CDCD)** with specific competence for clinical, cognitive behavioural assessment and therapeutic care (first system in Europe)

ASSESSMENT
(CANEVELLI ET AL., 2021)
(BACIGALUPO ET AL. 2023)

→ **Survey among CDCD** not homogeneously distributed in the country, not uniform assistance, different dagnostic patient journey and care pathway, dismogeneity in facilities and requirements

Dementia National Plan Started in **2014** // Funded in **2020**

«Piano nazionale demenze - Strategie per la promozione ed il miglioramento della qualita' e dell'appropriatezza degli interventi assistenziali nel settore delle demenze».
- Rep. atti n. 135/CU). (15A00130) (Di Fiandra et al., 2015) (G.U. Serie Generale , n. 9 del 13 gennaio 2015) (Ancidoni et al., 2022)

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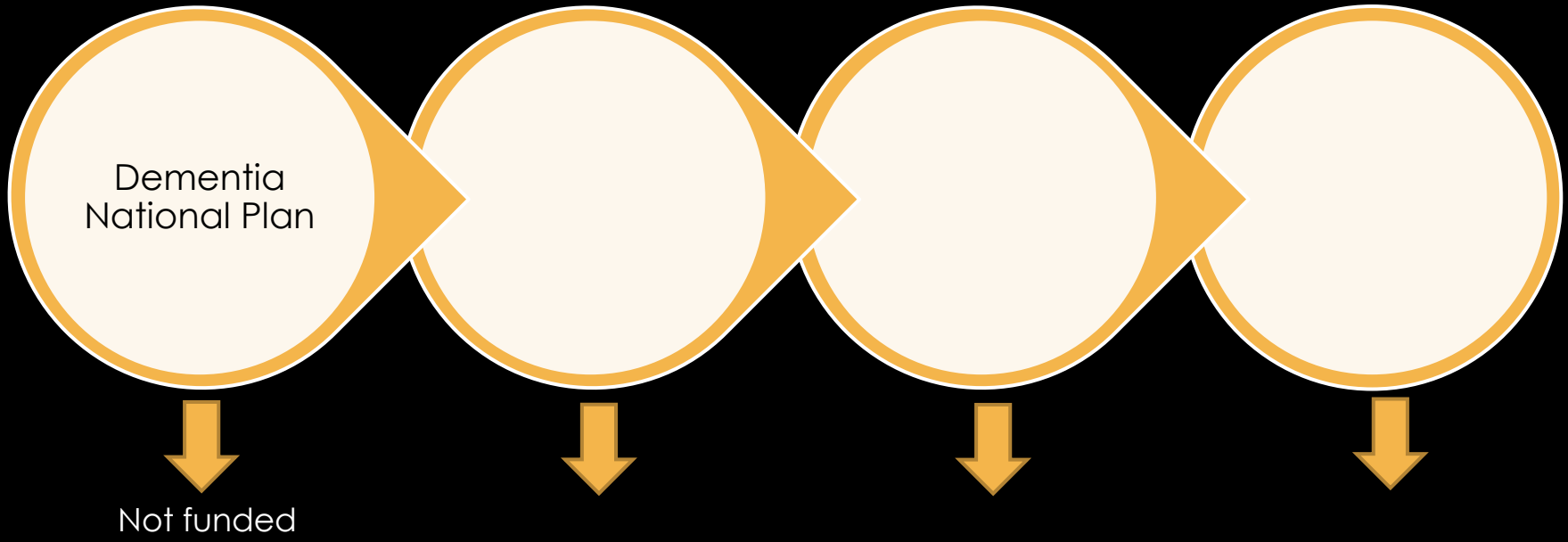

Dementia National Plan – Governance

Dementia National Plan 2014 (Di Fiandra et al., 2015)

Aims:

Standardize the quality/quantity of the service

Promoting Integration between services

Formulation of guidelines to be applied

Modality

Local authorities define coherent plans based on their mandates

Temporary Dementia Fund 2020 (Ancidoni et al., 2022)

15m Eu (5 x 3 anni)per:

Develop guidelines to support families and clients

Update PND

Implement PND

Promote epidemiological investigations.

Promoting prevention

Health profession training

National electronic register

Regional monitoring and evaluation

National Dementia Board 2017 renewed 2022 (Ministerial Decree 22.07.2022)

Actions:

Ensures PND monitoring and implementation

Composition:

5 technicians

21 Representatives of the Regions

2 Scientific Societies: SINDem, SIMG (MMG), AIP (Psgeriatrics)

2 Family and patients Associations

1 Ministry of Labour and Social Policies

1 AIFA

COURTESY OF M BOCCARDI.

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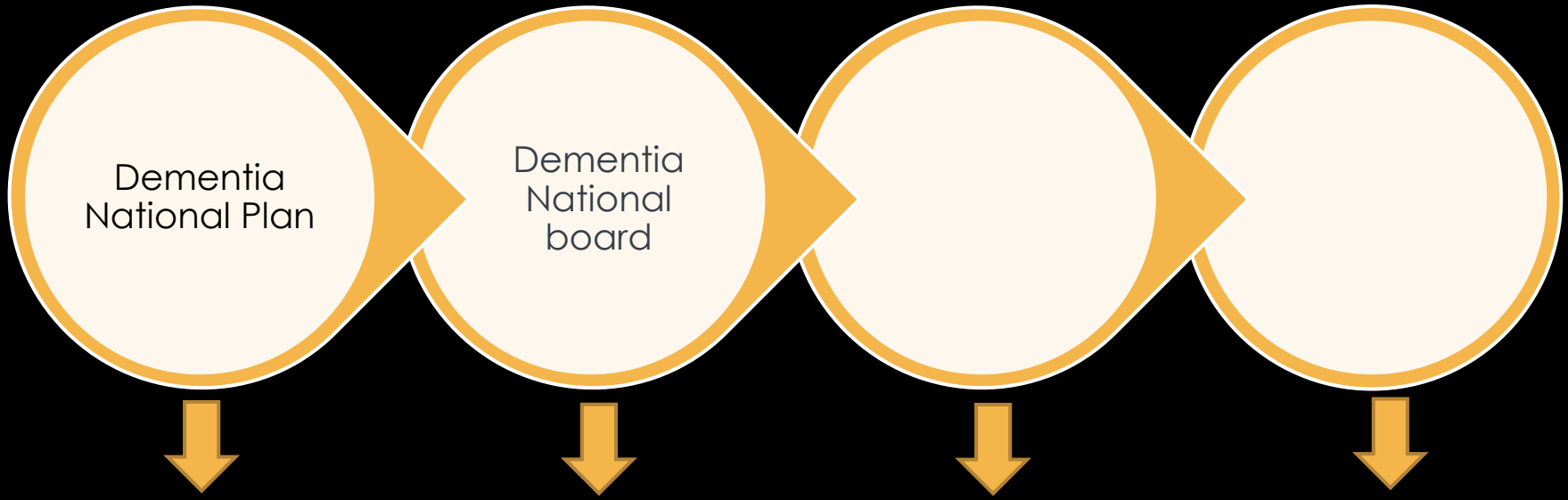

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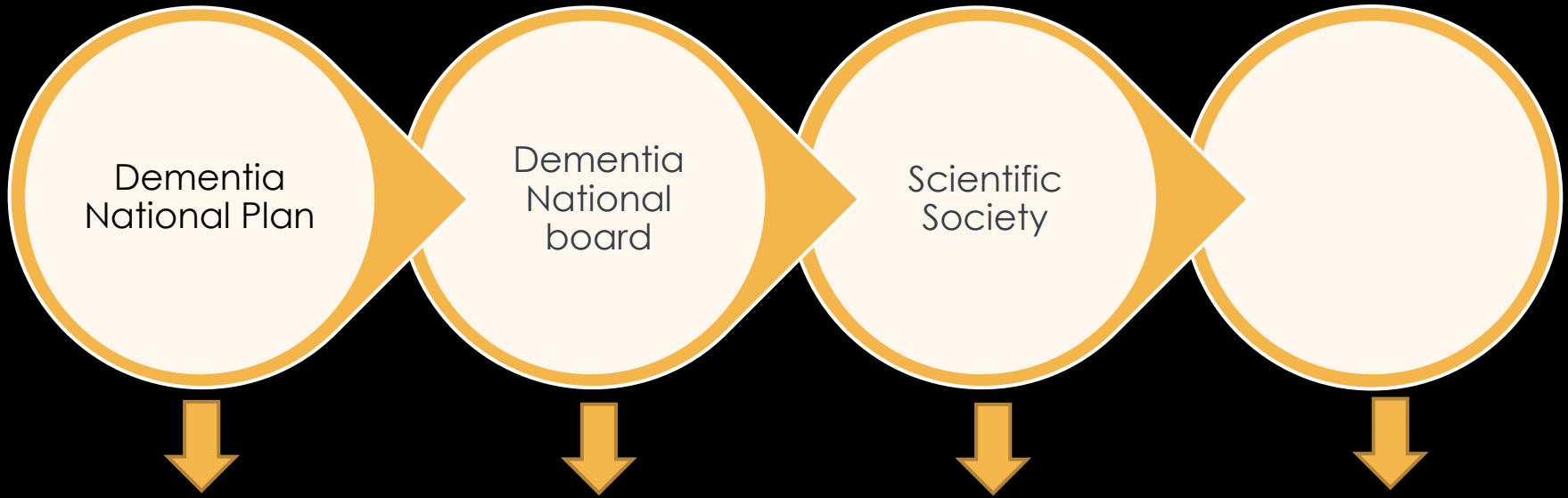

Neurological Sciences (2025) 46:2913–2923
https://doi.org/10.1007/s10072-025-08143-5

CONSENSUS PAPERS AND GUIDELINES

Towards a new Value-based scenario for the management of dementia in Italy: a SINdem delphi consensus study

Camillo Marra[1,2] · Fl… · Paolo Caffarra[4] · Federica L'Abb…
Laura Bonanni[11] · A…
Francesco Di Lorenz…
Benedetta Nacmias…
Fabrizio Tagliavini[25]
Marco Bozzali[28] · Or…

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 21 November 2024
DOI 10.3389/fneur.2024.1455787

OPEN ACCESS

Italian standardization of the BPSD-SINDEM scale for the …sychiatric …vith

…tonio[4,5†], Marta Zuffi[6], …Panigutti[4], …gio[8], Alfredo Costa[9], …zo[1,2,3*] and

Neurological Sciences (2025) 46:1617–1627
https://doi.org/10.1007/s10072-024-07863-4

ORIGINAL ARTICLE

Itel MMSE: a short phon… Validation study by the

Davide Quaranta[1,2,3] · Federica L'Ab…
Valentina Bessi[11,12] · Laura Bonanni…
Stefano F. Cappa[16,17] · Franco Giubi…
Roberto Monastero[23] · Francesca Fe…
Gioacchino Tedeschi[27] · Camillo Ma…

Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging

Roadmap to Alzheimer's Biomarkers in the Clinic

Biomarkers for the diagnosis of Alzheimer's disease in clinical practice: an Italian intersocietal roadmap

Giovanni B. Frisoni [a,b,j,*], Daniela Perani [c,d], Stefano Bastianello [e,f], Gaetano Bernardi [g,h], Corinna Porteri [a,i], Marina Boccardi [a,j], Stefano F. Cappa [k,l], Marco Trabucchi [m,n], Alessandro Padovani [o,p]

ORIGINAL ARTICLE

Italian consensus recommendations for a biomarker-based aetiological diagnosis in mild cognitive impairment patients

M. Boccardi[a,b], V. Nicolosi[a], C. Festari[a,c], A. Bianchetti[d,e], S. Cappa[a,f,g], D. Chiasserini[h,i], A. Falini[j,k,l], U.P. Guerra[m,n], F. Nobili[n,o,p], A. Padovani[g,q], G. Sancesario[l,r], S. Morbelli[o,p], L. Parnetti[s], P. Tiraboschi[t], C. Muscio[t], D. Perani[j,k], F.B. Pizzini[u], A. Beltramello[u,v], G. Salvini Porro[w], M. Ciaccio[i,x], O. Schillaci[y,z], M. Trabucchi[e,y], F. Tagliavini[t] and G.B. Frisoni[a,b]

…diagnosis of dementia with Lewy bodies (DLB) …entia Centers: a study by the Italian DLB study

Angelo Di Iorio[2] · Raffaello Pellegrino[2] · Amalia Cecilia Bruni[3] · …hiari[5] · Stefano Pretta[6] · Camillo Marra[7] · Maria Sofia Cotelli[8] · Andrea Arighi[9] · …ruzza[10] · Francesca Caso[11] · Cristina Paci[12] · Mara Rosso[13] · Serena Amici[14] · …tto[4] · Simona Luzzi[16] · Annalisa Castellano[17] · Fabrizia D'antonio[18] · …Tommaso Piccoli[21] · Marco Mauri[22] · Federica Agosta[23] · Claudio Babiloni[24,25] · …Massimo Filippi[23] · Daniela Galimberti[9,27] · Roberto Monastero[28] · …[0] · Daniela Perani[31] · Laura Serra[32] · Vincenzo Silani[33] · Pietro Tiraboschi[29] · …Padovani[4] · Laura Bonanni[2] · on Behalf of the Italian Dementia with Lewy bodies Study Group (DLB-SINdem)

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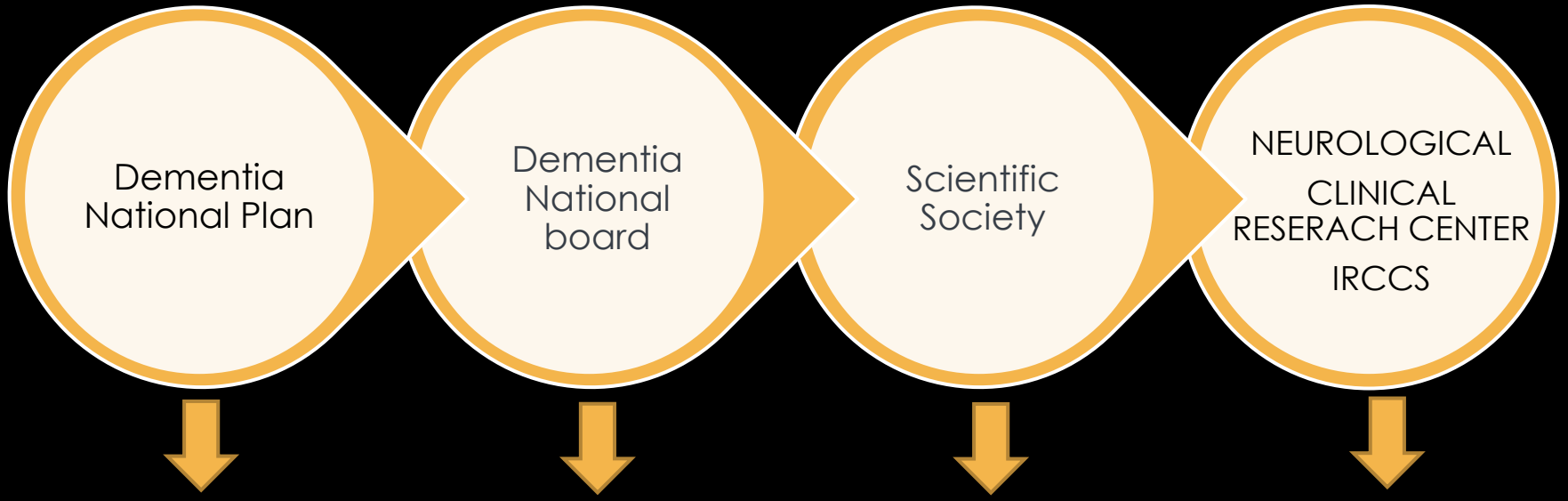
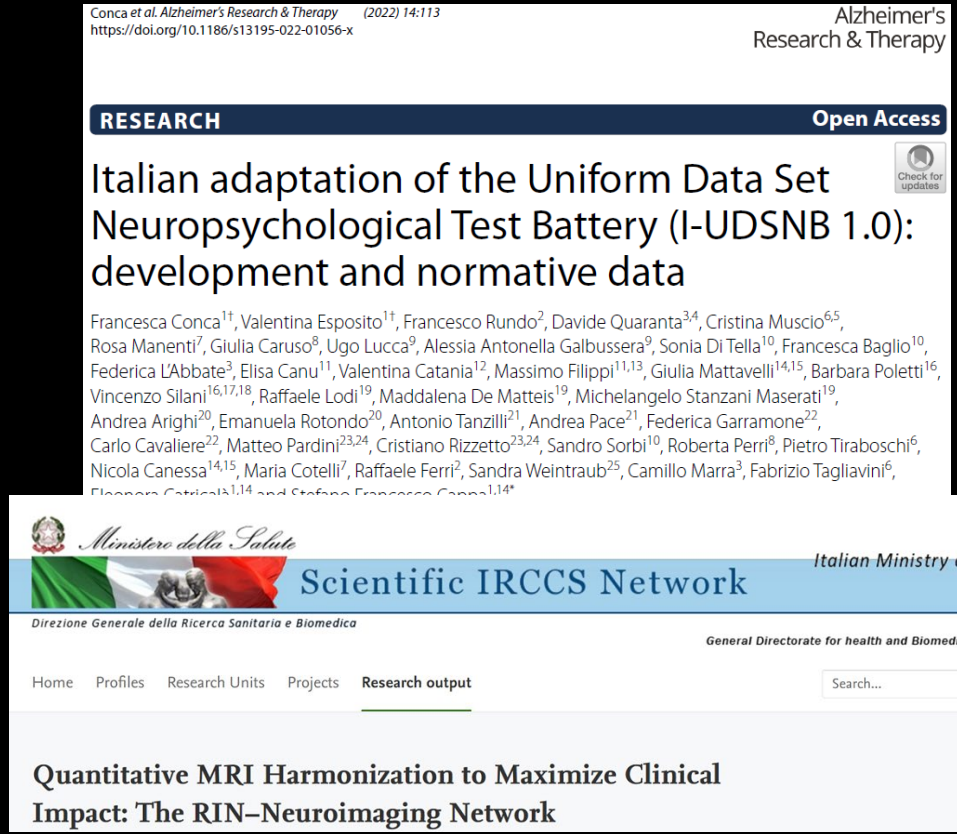


HARMONIZATION PROGRAMS

ITALIAN MINISTRY OF HEALTH RCR-2020-23670067 AND RCR-2021-23671214

CLINICAL HARMONIZATION PROGRAM AMONG RESEARCH CLINICS IN ITALY:

- *CLINICS*
- *NEUROPSICOLOGIY*
- *BIOMARKERS*
- *RADIOLOGY*
- *NUCLEAR MEDICINE*
- *GENETICS*



Conca *et al. Alzheimer's Research & Therapy* (2022) 14:113
https://doi.org/10.1186/s13195-022-01056-x

Alzheimer's Research & Therapy

RESEARCH Open Access

Italian adaptation of the Uniform Data Set Neuropsychological Test Battery (I-UDSNB 1.0): development and normative data

Francesca Conca[1†], Valentina Esposito[1†], Francesco Rundo[2], Davide Quaranta[3,4], Cristina Muscio[6,5], Rosa Manenti[7], Giulia Caruso[8], Ugo Lucca[9], Alessia Antonella Galbussera[9], Sonia Di Tella[10], Francesca Baglio[10], Federica L'Abbate[3], Elisa Canu[11], Valentina Catania[12], Massimo Filippi[11,13], Giulia Mattavelli[14,15], Barbara Poletti[16], Vincenzo Silani[16,17,18], Raffaele Lodi[19], Maddalena De Matteis[19], Michelangelo Stanzani Maserati[19], Andrea Arighi[20], Emanuela Rotondo[20], Antonio Tanzilli[21], Andrea Pace[21], Federica Garramone[22], Carlo Cavaliere[22], Matteo Pardini[23,24], Cristiano Rizzetto[23,24], Sandro Sorbi[10], Roberta Perri[8], Pietro Tiraboschi[6], Nicola Canessa[14,15], Maria Cotelli[7], Raffaele Ferri[2], Sandra Weintraub[25], Camillo Marra[3], Fabrizio Tagliavini[6],

Ministero della Salute

Italian Ministry of Health

Scientific IRCCS Network

Direzione Generale della Ricerca Sanitaria e Biomedica

General Directorate for health and Biomedical Research

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Quantitative MRI Harmonization to Maximize Clinical Impact: The RIN–Neuroimaging Network

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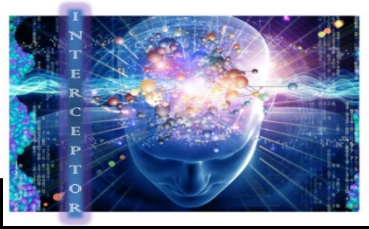
AGENZIA ITALIANA DEL FARMACO
Tutela Ricerca e Sviluppo per la Salute



ON THE EARLY DIAGNOSIS OF THE PRODROMAL STAGE OF ALZHEIMER DISEASE. THE PROGRESSION FROM MILD COGNITIVE IMPAIRMENT (MCI) TO DEMENTIA: THE ROLE OF BIOMARKERS IN THE EARLY INTERCEPTION OF PATIENTS TO WHOM PROVIDE FUTURE DISEASE-MODIFYING DRUGS

The primary aim of INTERCEPTOR is to identify a biomarker or a set of biomarkers able to predict with greatest accuracy, highest risks/costs ratio, lowest invasiveness and best availability on the territorial level, the conversion of diagnosis of MCI to dementia in a 3 years follow-up period.

This in order to initiate as soon as possible all those initiatives to contrast disease progression.

The secondary aim is to define an optimal organizational model, both in terms of transferability in clinical practice of diagnostic path defined of the primary objective and the sustainability of costs, to identify patients able to prescription of antidementia drug that now are in the course of experimentation by RCTs.

THE ARRIVAL OF ANTI-AMYLOID DRUGS: OPPORTUNITIES AND LIMITATIONS

A THERAPEUTIC REVOLUTION BETWEEN BENEFITS AND RISKS

- **New therapeutic phase:** **Monoclonal antibodies** pave the way for potential disease-modifying treatments, targeting the neurobiology of AD.
- **Demonstrated moderate efficacy over the timeframe of clinical trials:** **- 27%** cognitive decline with **lecanemab** and **−35%** with **donanemab** in selected patients, especially at the **MCI stage**.
- **Relevant clinical risks** : Frequent **ARIAs**, especially in **ApoE ε4** carriers, require serial **monitoring with MRI** and expert centers
- **Significant organisational and economic impact** on the **NHS**.

EUROPEAN REGULATORY FRAMEWORK AND IMPLICATIONS FOR ITALY

RIGOUR, APPROPRIATENESS AND ORGANISATIONAL CHALLENGES

EMA 2025 Decisions
Lecanemab authorised at EU level for early Alzheimer's disease; donanemab approved after re-examination.

Strict conditions of use
Use limited to patients with **early diagnosis** and **biomarker -based confirmation** ; intensive monitoring with **MRI** and **ApoE** genetic testing.

Italian challenge
Need for up-to-date **national registries** , accredited **prescribing centers (CDCD level 3)**, and **PDTAs** to ensure equity and sustainability.

CHALLENGES IN THE ITALIAN SYSTEM

THE ITALIAN CONTEXT

THE PROCESS OF IMPLEMENTATION IN THE REAL WORLD

- THE TRANSLATION OF THERAPIES INTO REAL-WORLD CLINICAL PRACTICE REQUIRES **A PRECISE REDEFINITION OF DIAGNOSTIC AND CARE PATHWAYS, THE ESTABLISHMENT** OF **STANDARDIZED MONITORING PROTOCOLS, AND ROBUST ORGANISATIONAL FRAMEWORKS** TO ENSURE ACCESS **EQUITY** AND PATIENT **SAFETY**
- THE **ITALIAN CONTEXT** PRESENTS WITH SPECIFIC CHALLENGES**. THE CURRENT NATIONAL DEMENTIA GUIDELINES, PUBLISHED BEFORE THE APPROVAL BY EMA OF ANTI-AMYLOID MONOCLONAL ANTIBODIES**, RECOMMEND **BIOMARKER-SUPPORTED DIAGNOSIS** IN **INDIVIDUALS WITH DEMENTIA ONLY** AND PROVIDE A **STRONG NEGATIVE RECOMMENDATION** FOR THEIR USE **IN MILD COGNITIVE IMPAIRMENT**
- **THE ITALIAN HEALTHCARE SYSTEM IS UNDERGOING REORGANIZATION UNDER THE MINISTERIAL DECREE 77/2022 (DM77)**, WHICH DEFINES NEW STANDARDS FOR COMMUNITY-BASED CARE. DM77 ESTABLISHES "**COMMUNITY HOMES**" AS MULTIDISCIPLINARY HUBS **FOR MANAGEMENT OF CHRONIC DISEASE**, AND STRENGTHENS THE **INTEGRATION BETWEEN PRIMARY CARE AND SPECIALIST SERVICES**

THE CDCD NETWORK AND MINISTERIAL DECREE 77

HOSPITAL-COMMUNITY INTEGRATION FOR INNOVATIVE DRUGS

Role of CDCDs
Centers for Cognitive Disorders and Dementia as fundamental nodes for diagnosis, management and follow-up.

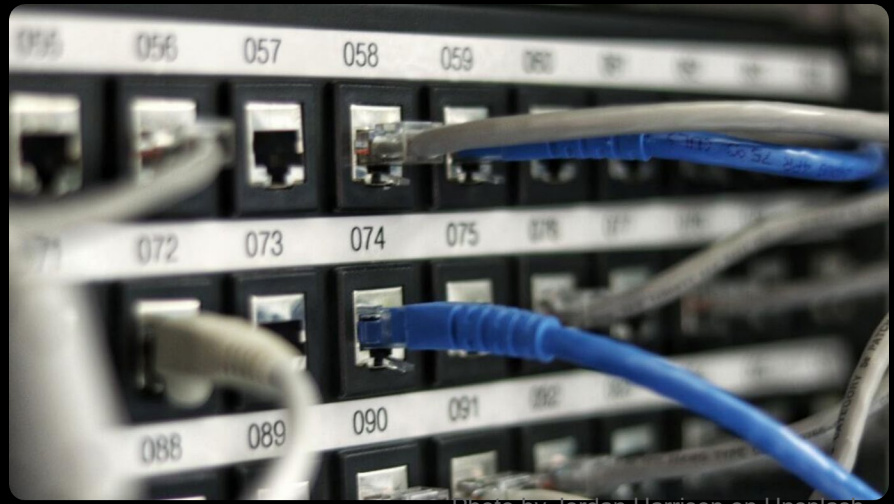
Integration with DM 77
The new structure of territorial assistance enhances the CDCDs and strengthens their function in the proximity model.

Prescribing centers
For anti-amyloid drugs, only level 3 CDCDs, equipped with multidisciplinary expertise and advanced technologies, will be approved for DMT prescription monitor.

HUB-AND-SPOKE JOURNEY AND SPECIALIST ROLES

AN INTEGRATED ORGANIZATIONAL MODEL FOR THE MANAGEMENT OF ALZHEIMER'S

- **Referral hub**: Highly specialized centers (CDCD level 3) with multidisciplinary skills, advanced diagnostics and complication management capabilities.
- **Territorial spokes** : GPs, neurologists and geriatricians in the area to guarantee early interception, triage and follow-up, in connection with the hubs.
- **Integrated network:** The structured collaboration between hub and spoke ensures equity of access, appropriateness and continuity of care.



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HEALTH TECHNOLOGY ASSESSMENT AND SUSTAINABILITY SCENARIOS

INTERNATIONAL EXPERIENCES AND CHALLENGES FOR ITALY

- **International experiences** : USA (Medicare), UK (NICE), France and Germany have adopted differentiated approaches for access and reimbursement, with HTA models and national registries.
- **Challenge for Italy:** Need to build an **interoperable national registry** , **accredited prescribers** and innovative **reimbursement models** (e.g., payment by results).
- **Complex balance:** The introduction of anti-amyloid drugs requires balancing **innovation** , **equity** of access, and **economic sustainability** .

CHALLENGE FOR ITALY: REGISTERS AND REIMBURSEMENT MODELS

GOVERNANCE TOOLS FOR EQUITABLE AND SUSTAINABLE ACCESS

- **Interoperable national registry:** Essential for collecting real-world data on efficacy and safety, ensuring transparency and continuous monitoring.
- **Accredited Prescribing Centers:** Key role of Level 3 CDCDs, equipped with **multidisciplinary teams** and **advanced diagnostic capabilities** .
- **Innovative reimbursement models:** Tools such as payment by results can balance equity of access and sustainability of the SSN.

THE ROLE OF CAREGIVERS IN THE THERAPEUTIC PATH

A PILLAR OF THE CARE SYSTEM

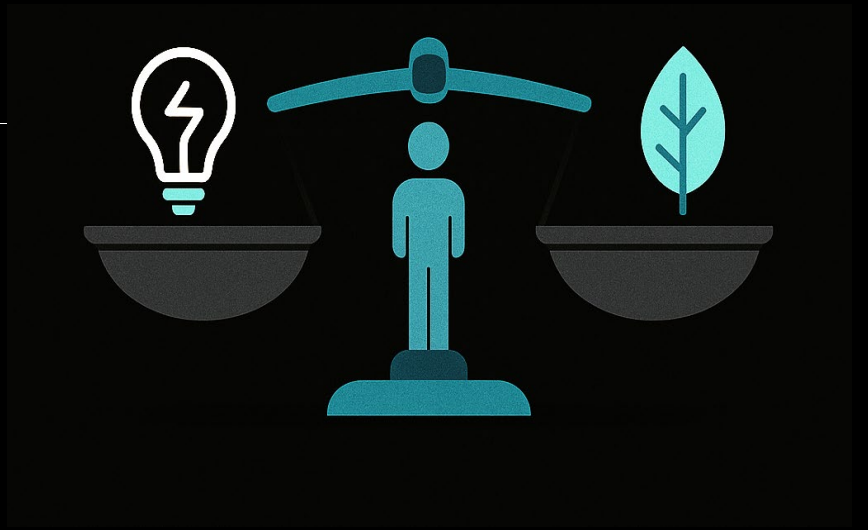
- **Essential support**: In Italy, more than 80% of assistance to people with Alzheimer's is guaranteed by family caregivers.
- **Complex needs:** High emotional, psychological, and economic burden, often with **a risk of burnout** and social isolation.
- **Enhancement of the role** : We need psychological support programs, training and dedicated economic support.
- **Outcome indicators:** PROMs and PREMs include the caregivers' point of view, which is essential for measuring the real impact of care.

Photo by Bruno Aguirre on Unsplash

BALANCING INNOVATION, EQUITY AND SUSTAINABILITY

NECESSARY CONDITION FOR THE ADOPTION OF ANTI-AMYLOID DRUGS

- **Therapeutic innovation** : New anti-amyloid therapies require a **paradigm shift** , offering unprecedented opportunities for early-stage patients.
- **Equity of access**: It is necessary to ensure **territorial uniformity** , avoiding that only some regions or centers can offer drugs.
- **Economic sustainability:** The high cost and monitoring requirements pose a risk to the financial stability of the NHS.
- **Integrated governance:** Only a careful balance between these elements will be able to translate innovation into value for the health system.



UNMET NEEDS

- New definition of helathcare pathway according to the different patients characteristics (es early onset dementia)
- To define a shared patient journey and Harmonized tools for Biological diagnosis
- To engage, and train the main health operators and to get full reliability of the present CDCD organization : which minimal requirements are madatory for the CDCD that will administer new DMT?
- To foresee the amount of potential subjects candidate to the new DMT in order to better define the distribution of highest specailized CDCD on the territory
- To plan an appropriate monitoring of patients under therapy in order to provide any needs for monitoring therapies efficacy and side effects (ARIA, IRR)

RESEARCH AND FUTURE PROSPECTS

TOWARDS NEW FRONTIERS IN THE FIGHT AGAINST AD

Pragmatic trials
Necessary to evaluate the efficacy of innovative drugs in real-world contexts and on heterogeneous populations.

Emerging biomarkers
Plasma tests (ptau217,NfL, GFAP) represent a potential game-changer for screening and early diagnosis.

Multimodal approach
Combination of pharmacological, digital therapies and prevention interventions to maximize the benefits.

Italy's role
Our country has the opportunity to strengthen its contribution to international clinical research.

CONCLUSIONS AND RECOMMENDATIONS

IS ITALY READY FOR ANTI-AMYLOID DRUGS?

NOT YET BUT

Historic opportunity

New therapies offer a paradigm shift, but only if integrated into an organized and resilient system.

Open criticalities

Territorial inhomogeneity, need for registries, qualified prescribing centers and intensive monitoring.

Enabling conditions

Prevention, updated PDTAs, enhancement of caregivers and digital innovation are essential pillars.

Integrated vision

Strong national governance to ensure equity, appropriateness and sustainability of the NHS.

Thank you for your kind attention