InRAD: Driving International Collaboration for Real-World Evidence in the Era of Novel Therapies and the Evolving Natural History in Alzheimer's Disease

International Registry for Alzheimer's disease and other Dementias (InRAD)

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Disclosures

- JV is a consultant for InRAD
- InRAD is coordinated by the independent International Registry for Alzheimer's Disease and Other Dementias Foundation, a health-related not-for-profit entity incorporated in the Netherlands
- InRAD has received financial contributions from the pharmaceutical industry, including Eli Lilly, Eisai, Roche, Schwabe Group, Novo Nordisk, Bristol Myers Squib, Biogen
- InRAD does not endorse any companies or products
- InRAD is operated independently from these companies
- Others partners include: Alzheimer's Network, Icometrix NV, Neurophet

https://www.inradnetwork.org/pharma-funding

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A Pivotal Moment for a Unified Approach

JB1

The International Registry for Alzheimer's Disease and Other Dementias (InRAD)

- Why InRAD?
  - Addressing the Gaps in Real-World Data
- What is InRAD?
  - Minimum Data Set (MDS) and Extended Data Set (EDS)
  - The InRAD cloud-based registry data entry platform
- Use case: Real-World Evidence for Value-Based Decisions
  - The AURORA-AD natural history sub-study

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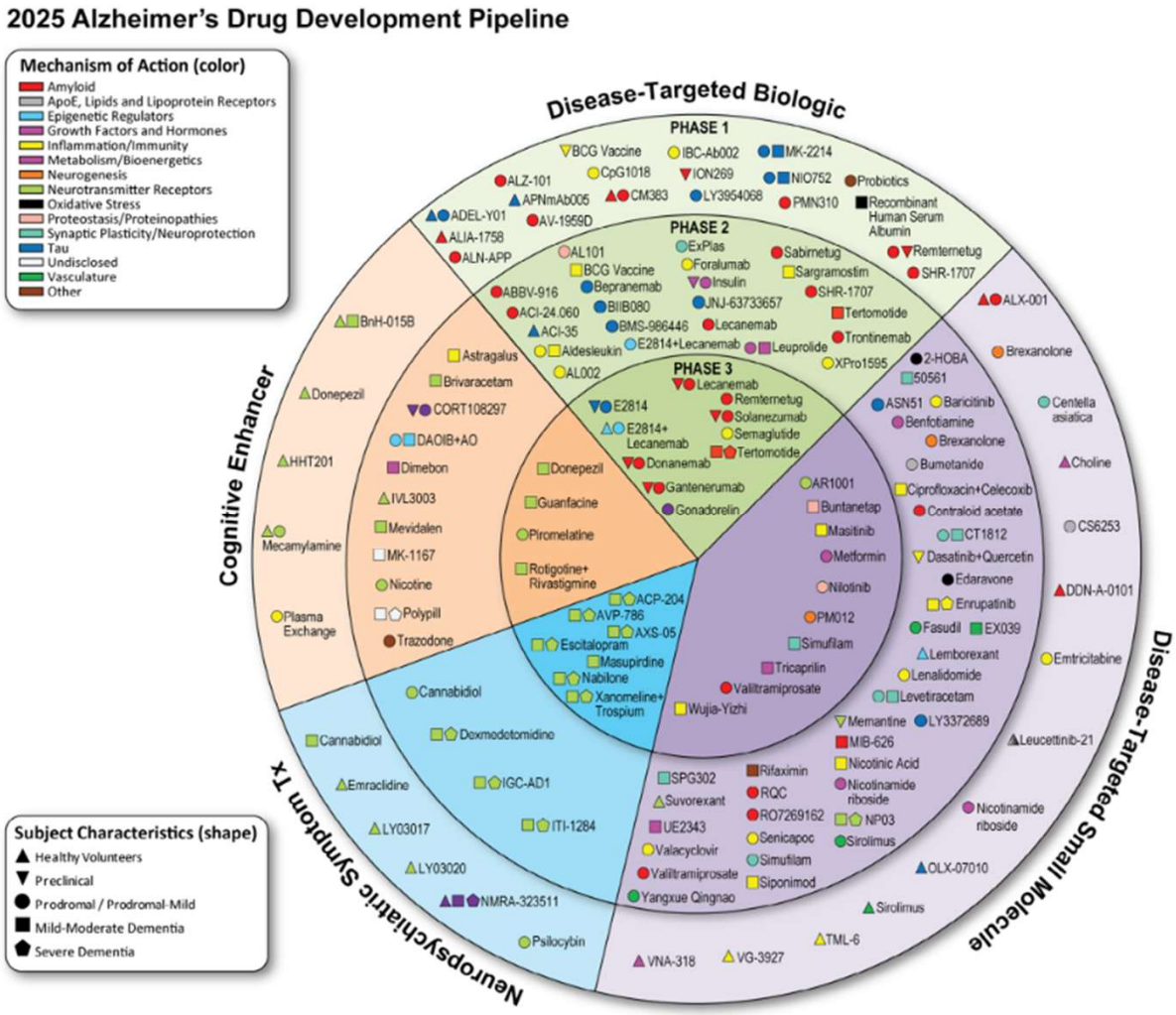
Slide 3

JB1 Here or elsewhere as appropriate I would make it clear this is a disease registry, not treatment. Would help clarify slide 5
Johan van Beek, 2025-11-10T14:12:38.589

AD care evolving rapidly

- Rich drug development pipeline
  - 138 drugs in development, Jan 2025[1]
  - Lecanemab, Donanemab
- Advances in biomarkers, diagnosis and prognosis evolving at fast pace[2]
- Lots of questions to be answered with the foundation of RWD[3-4]
  - New early AD natural history
  - Application of biomarkers & risk factors
    - Earlier diagnosis?
  - Long-term safety, effectiveness, value of treatments
  - … and many others



AD: Alzheimer's disease. RWD: Real-World Data. EMRs: Electronic Medical Records

1. Cummings et al. Alzheimer's Dement 2025;11:e70098. 2. Hansson et al. Nat Aging. 2023;3(5):506-519. 3. Dang A. Pharmaceut Med. 2023;37(1):25-36). 4. Miller et al. Front Aging. 2023:4:1179275

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Enabling Comparative Health and Value Assessment

- **Natural History & Prognostic Modelling**
  - Disease progression & prognostic factor studies
  - Subgroup analyses disease trajectory in underrepresented populations
- **Real-World Outcomes & Quality of Care**
  - Treatment Sequencing & Switching Patterns
  - Biomarker validation
  - Signal detection, **Long-term Safety and Effectiveness**
  - Quality-of-Care Benchmarking
    - Compare adherence to clinical guidelines across centres and countries.
- Effectiveness Research
  - Comparative effectiveness studies
  - Early vs Delayed diagnosis and treatment
- Patient-centred & preference studies
  - Patient preference eg SC vs IV, QoL, PROs
  - Shared decision making & adherence/persistence
- Regulatory & Post-Authorization Studies
  - CAP/PAES/PASS including Risk Minimisation Plan effectiveness
  - Slower titration/different dosing regimen
- **Health Economics & Resource Utilization**
  - Cost-effectiveness: National reimbursement, Risk-Sharing Scheme Evaluation, sub-groups
  - Time & Motion studies

InRAD supports many use cases including long-term safety and effectiveness & health economics

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GU1

InRAD: Addressing the Gaps in Real-World Data

- EMRs are not designed or standardised for research
- Multiple fragmented data sources exist, many at the “centre level”
- Data from existing cohorts do not follow a common data model fit for treatment follow up
  - e.g. standard outcomes or safety medical events
- “Diagnose and Adiós”: Focus has been on diagnosis but not longitudinal follow up and practice is changing
- No international disease registries exists for generalisable real-world evidence generation
- Sustainable and consistent investment in disease registries at the national and internation arena does not exist

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Slide 6

GU1 I strongly dislike the phrase diagnose and adios - I feel it's flippant and disrespectful to the doctors who care for their patients. Can we stop using it?

Guest User, 2025-11-10T14:17:35.805

InRAD, the first and only international clinical practice-based registry in AD

Meaningful data | **Sustainable platform** | **Collaborative science**

- Free-to-access cloud-based data platform and collaboration infrastructure
- Contributing doctors' centres own their data (Data Controller)
- Collaboration within and outside the network
- InRAD (Data Processor) coordinates international research and studies
- Participation in scientific agenda (e.g. own research; multicentre or national research studies)
- Data Quality workstream to support use cases

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First step: reaching consensus on MDS/EDS

- Define **Minimum Data Set** (MDS) for Alzheimer's disease diagnosis and care
- Provide **Extended Data Set** (EDS) to enrich medical context
  - International Steering Committee
  - Multistakeholder consultation: clinicians & academics, patient representatives, pharmaceutical industry
  - Consensus agreement & Publication

Minimum data set (MDS)

- Demographic, efficacy and safety data collected by every investigator

Extended data set (EDS)

- Collected data collected where practice permits, certain instruments are used (e.g. those mandated by local authorities or that are part of local clinical practice) or when sites participate in registry studies

Perneczky et al. Real-world datasets for the International Registry for Alzheimer's Disease and Other Dementias (InRAD) and other registries: An international consensus, The Journal of Prevention of Alzheimer's Disease 2025 https://doi.org/10.1016/j.tjpad.2025.100096

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From AD/PD 2025 presentation
https://www.inradnetwork.org/resources

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Consensus sponsors and partners

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MSBase Neuro-Immunology Registry
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Minimum Data Set – InRAD Observational Study Protocol

Section	Field	Definition	Frequency	
			Entry Visit	Visit (minimum Annually)
Patient Profile/ Demographics	Name®/Patient ID	Patient globally unique ID for registry (created by system)	X	
	Consent for registry	N/Y, Date given / date withdrawn (Y required for registry participation)	X	
	Sex at birth	M/F/other/Not specified	X	
	Birth date	Year and month only sent to registry	X	
	Ethnicity#		X	
	Place of residence	Country	X	
	Education	ISCED 2011	X	
	Height	cm	X	
	Weight	Kg	X	X
Disease characteristics (diagnostic work-up)	Medical History	Relevant medical conditions (history and concomitant)&	X	X
	Family History of Dementia	First degree relative/dementia type	X	
	Date of first consultation for screening for dementia	Date	X	
	Date of symptom onset	Date	X	
	Predominant Symptoms/Syndrome	No specific syndrome/amnestic/Posterior cortical/ frontal/primary progressive aphasia/other atypical presentations	X*	
	Date of diagnosis	Date and service	X*	
	Diagnosis	Alzheimer Disease plus others (from picklist)	X*	
	Amyloid status	Positive/negative/Indeterminant/not done	X*	
	Tau status	Positive/negative/Indeterminant/not done	X*	
	Genetic status	Positive/negative/VUS/not done for PSEN1,PSEN2, APP and APOE	X*	
	Imaging evidence of neurodegeneration or other findings	Atrophy/hypometabolism: normal/abnormal/Indeterminant/not done	X*	
Clinical outcomes	Cognitive screening test	N/Y (MoCA or MMSE; Test date, Test version, Score)	X	X
	Clinical staging$	Asymptomatic (not AD); Asymptomatic, deterministic gene (0); Asymptomatic, biomarker evidence only (1); Transitional decline (2); Mild Cognitive impairment (3); Mild (4); Moderate (5) or Severe dementia (6)	X	X
	Milestone events	Living/Driving /working status	X	X
	Functional Scales	Y/N	X	X
Safety and relevant medical condition	ARIA	N/Y, medical event report (E/H or ICH>1cm)		X
	Other Medical Events (e.g. Serious Adverse Event (SAE) or other events of interest)	Untoward medical occurrence (e.g., death, hospitalisation, illness resulting in major change)		X
	Infusion/injection reaction	N/Y, medical event report		X
	Specified medical events of interest	Serious malignancy, serious infection, other neurological conditions		X
	Medical History conditions&	Relevant medical conditions (history and concomitant)	X	X
Imaging	MRI	N/Y – type, date of scan and reason • Diagnosis • Clinical Follow-up • ARIA Monitoring • Other	X	X
Treatments	AD specific treatment	Treatment ID, name, start/stop date	X	X
	Cognitive treatments of interest	Treatment ID, name, start/stop date	X	X
	Other treatments of interest (Pharmacological and non-pharmacological)	Treatment ID, name, start/stop date	X	X
Registry discontinuation	Including death	Date and cause of death		X

https://clinicaltrials.gov/study/NCT07213700

Adapted from Perneczky et al. Real-world datasets for the International Registry for Alzheimer's Disease and Other Dementias (InRAD) and other registries: An international consensus, The Journal of Prevention of Alzheimer's Disease 2025
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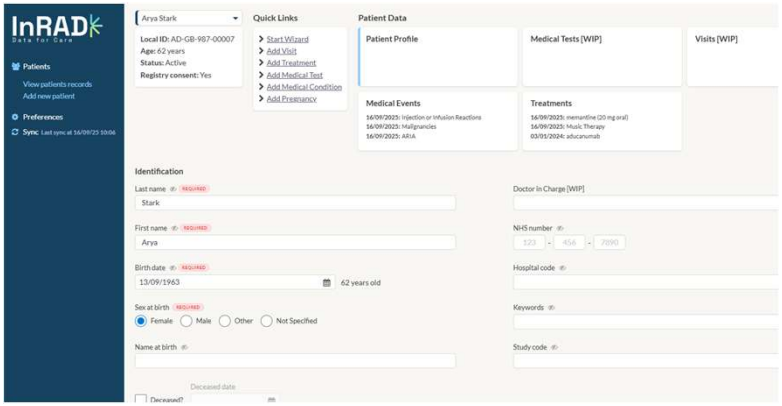
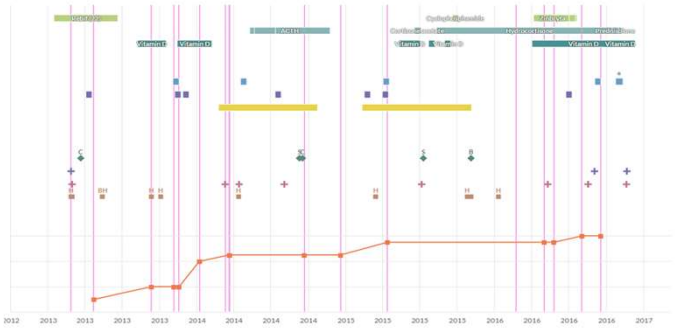
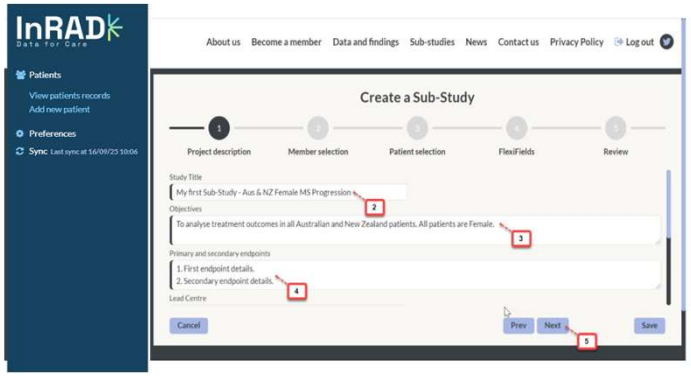
Reducing the Data Collection Burden
By Leveraging 20+ years of MSBase registry expertise







Data entry system

- Web-based
- Intuitive, roll-out menus
- Access through patient profile, disease ‘sections’
- PDF-extractable summary reports for patient EMRs

Patient Overview Graph

- Increased functionality at point-of-care
- Valued by clinicians to enable day-to-day patient management as well as accessible clinic data management

Registry and collaboration

- Tool for Investigator-initiated prospective ‘sub-studies’
- Filtering for defined sub-set of patient records
- Allows for the creation of national/regional sub-studies

User-friendly interface
Designed to fit clinical workflow,
Minimising extra work for doctors

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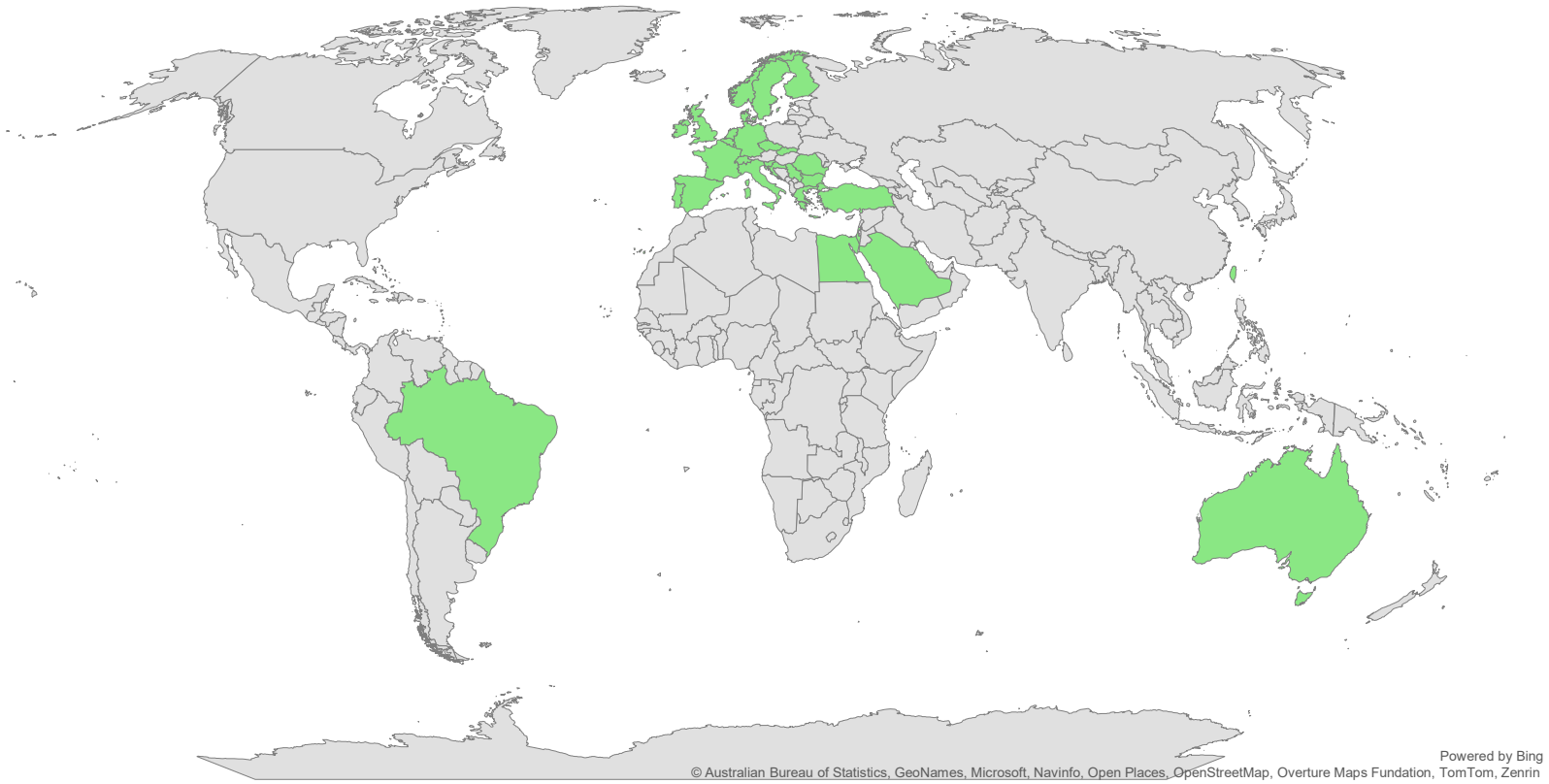
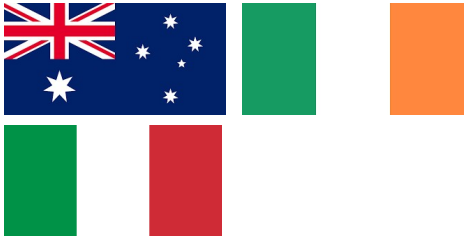
Launching InRAD Around the World



PILOT - November 2025



Wave 1 deployment
January 2026
18 countries
27 PIs

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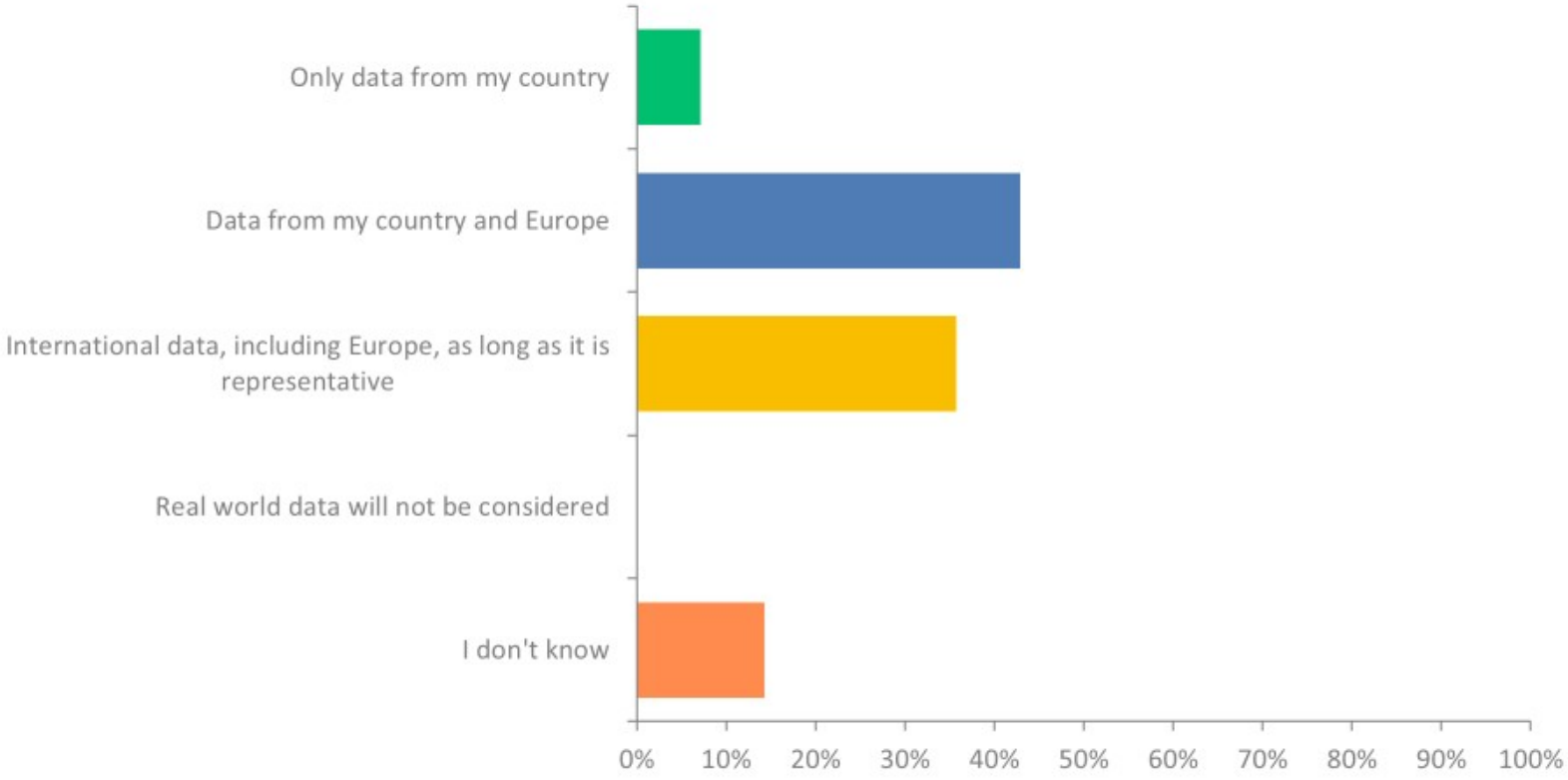
Q9: What source of real world data do you anticipate your country's reimbursement authority (HTA) will consider in the evaluation of new therapies?

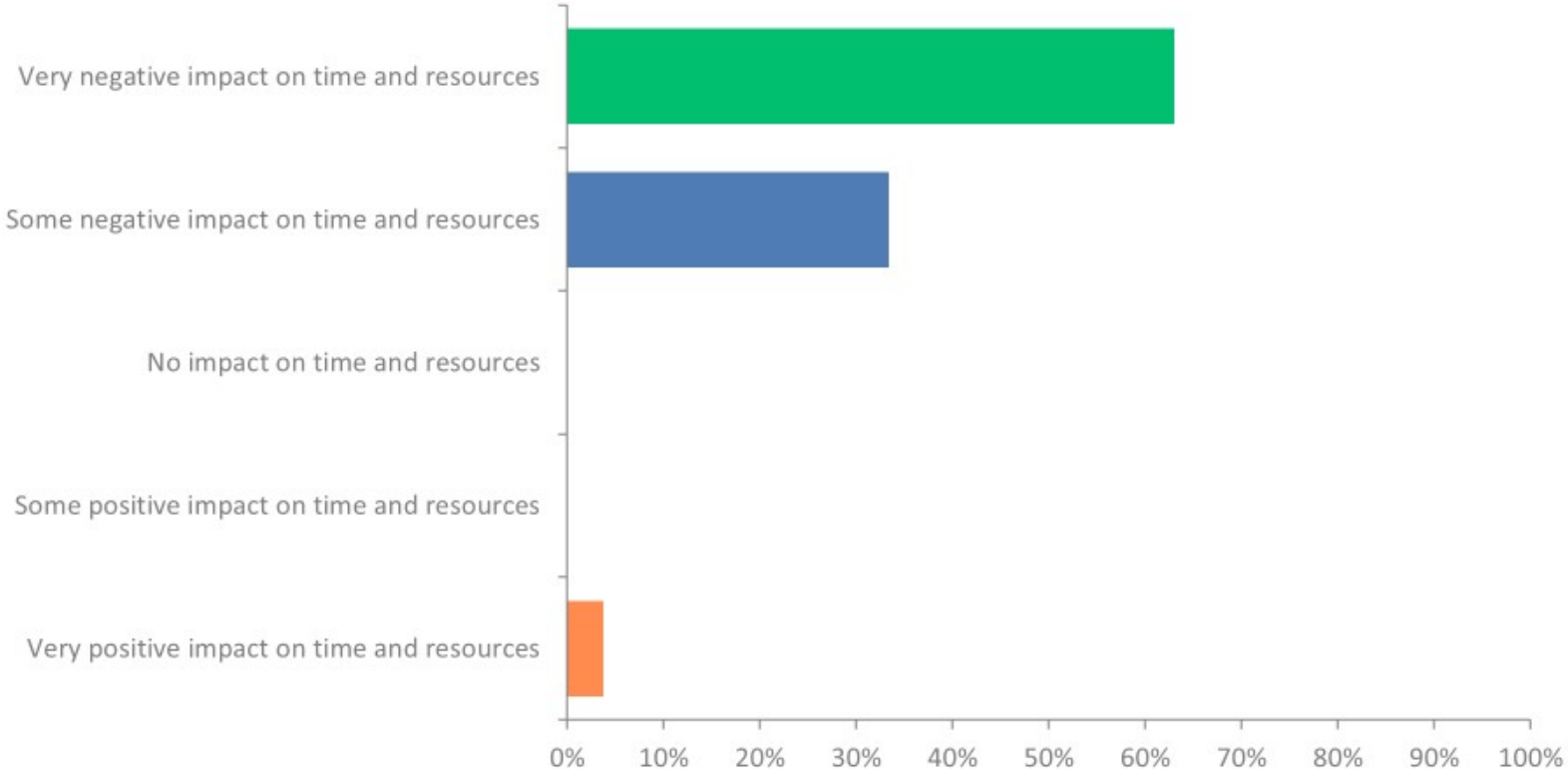


Answered: 28 Skipped: 0

Results as of 7/11/2025

InRAD Data for Care

Q11: What impact would it have on your clinical services (time/resources) if each pharmaceutical company collects real world data for each drug for post-authorisation safety and effectiveness studies (regulatory), HTA and clinical insights using different data collection platforms / registries and protocols?



Answered: 27 Skipped: 1

Results as of 7/11/2025

InRAD Data for Care

Collecting the Right Data—Not Just Any Data

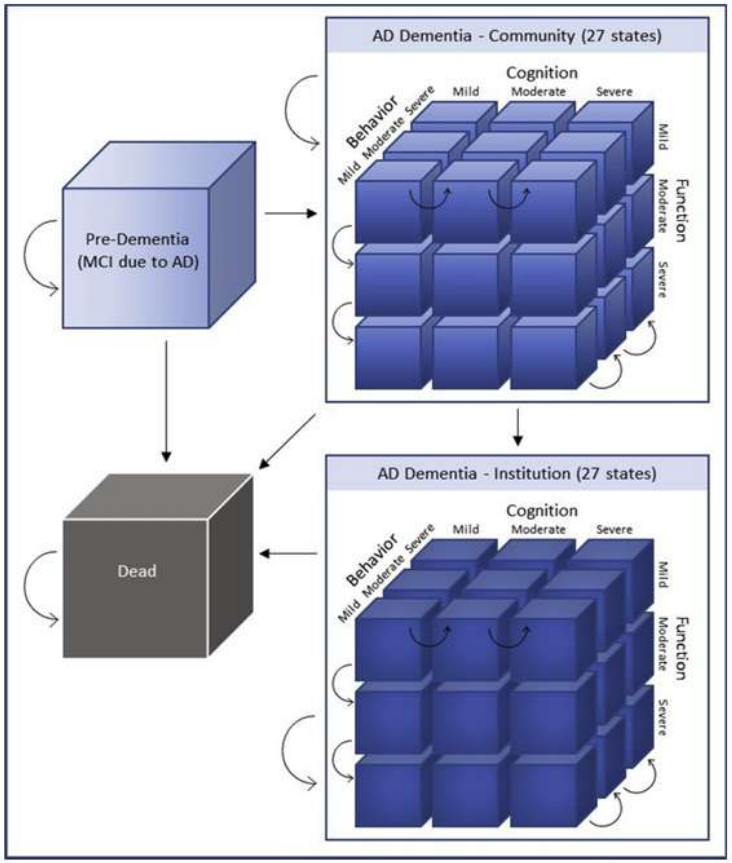


Fig. 1. Schematic for AD model of disease progression. Abbreviations: MCI, mild cognitive impairment; AD, Alzheimer's disease.

Table 2
Descriptive system for AD: Definition by level of severity for each symptom domain

Domain	Severity level	Label	Definition	
Cognitive function	Mild	[1]	$21 \leq$ MMSE ≤ 26	MDS
	Moderate	[2]	$10 \leq$ MMSE ≤ 20	
	Severe	[3]	$0 \leq$ MMSE ≤ 9	
Behavior & mood	No problem/mild	[1]	NPI-Q: each item ≤ 1	EDS
	Moderate	[2]	NPI-Q: each item ≤ 2; with at least one item equal to 2	
	Severe	[3]	NPI-Q: at least one item equal to 3	
Functional ability	No problem/mild	[1]	$0 \leq$ FAQ total ≤ 8	EDS
	Moderate	[2]	$9 \leq$ FAQ total ≤ 23	
	Severe	[3]	$24 \leq$ FAQ total ≤ 30	

Abbreviations: AD, Alzheimer's disease; MMSE, Mini-Mental State Examination; NPI-Q, neuropsychiatric inventory questionnaire; FAQ, Functional Assessment Questionnaire.

InRAD allows essential data to be captured for research and reimbursement.

Green et al. Assessing cost-effectiveness of early intervention in Alzheimer's disease: An open-source modelling framework. Alzheimer's & Dementia 2019. https://doi.org/10.1016/j.jalz.2019.05.004

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AURORA-AD

A prospective, observational, InRAD registry-led sub-study, to shed light on the progression and transitions of Alzheimer's disease, and burden on patients, care partners, and healthcare systems

Evaluating the natural history of Alzheimer's disease in the emerging setting of disease-modifying treatments and timely and accurate diagnosis supported by biomarkers

Study Type	Prospective, Observational, InRAD registry-led registry substudy
Primary objective	Define global disease trajectories (time to transition between AD stages)
Secondary objectives	• Characterize cognitive trajectories and their interactions with clinical and biomarker risk factors • Assess disease burden on patients, caregivers, and healthcare systems (resource utilization) • Explore the impact of comorbidities and concurrent treatments on disease progression
Exploratory Objectives	• Identify high- and low-risk progression profiles • Examine blood biomarkers for early diagnosis and progression prediction • Evaluate patient (and care partner)-electronic PROs • Evaluate digital solutions for cognitive assessment for early diagnosis • Investigate imaging biomarkers (e.g. MRI mediotemporal lobe atrophy) as predictors of deterioration
Patient population	Patients from first presentation to health services and diagnosis
Enrollment	TBC
Study duration	5 years TBC
Locations	AURORA-AD serves as an umbrella protocol. Will run across Europe with ca. 30 EADC sites + Others TBC

Doctors need time & motivation!

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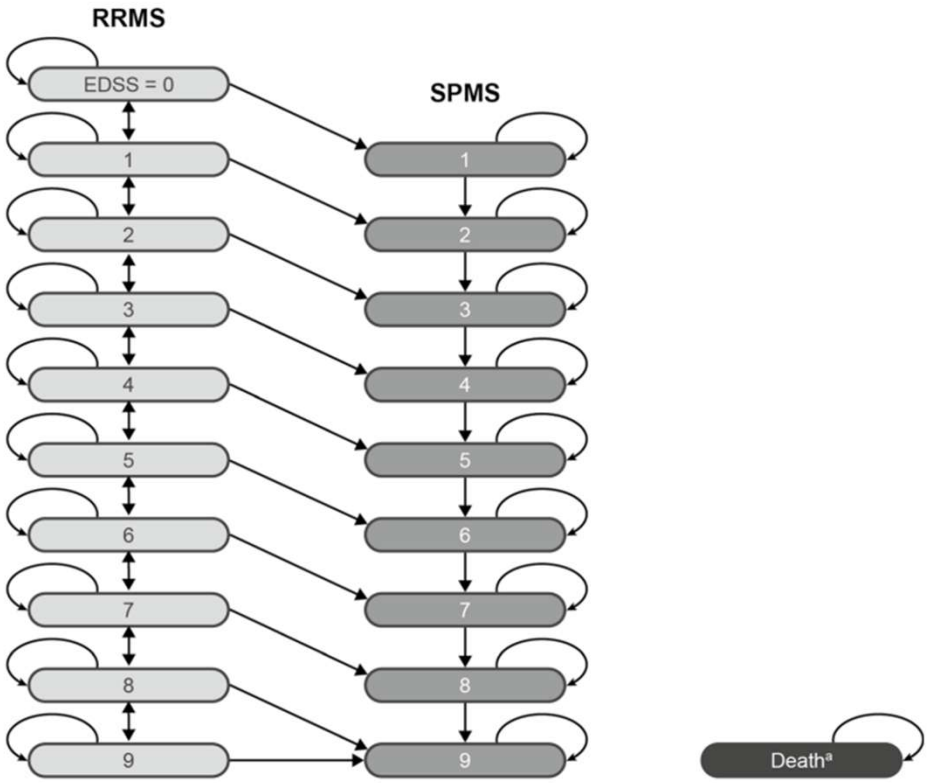
Real-World Evidence for Value-Based Decisions

PharmacoEconomics (2022) 40:323–339
https://doi.org/10.1007/s40273-021-01106-6

ORIGINAL RESEARCH ARTICLE

Comparative Effectiveness and Cost-Effectiveness of Natalizumab and Fingolimod in Patients with Inadequate Response to Disease-Modifying Therapies in Relapsing-Remitting Multiple Sclerosis in the United Kingdom

Timothy Spelman[1] · William L. Herring[2] · Yuanhui Zhang[2] · Michael Tempest[3] · Isobel Pearson[4] · Ulrich Freudensprung[5] · Carlos Acosta[6] · Thibaut Dort[6] · Robert Hyde[5] · Eva Havrdova[7] · Dana Horakova[7] · Maria Trojano[8] · Giovanna De Luca[9] · Alessandra Lugaresi[10,11] · Guillermo Izquierdo[12] · Pierre Grammond[13] · Pierre Duquette[14] · Raed Alroughani[15] · Eugenio Pucci[16] · Franco Granella[17] · Jeannette Lechner-Scott[18] · Patrizia Sola[19] · Diana Ferraro[20] · Francois Grand'Maison[21] · Murat Terzi[22] · Csilla Rozsa[23] · Cavit Boz[24] · Raymond Hupperts[25] · Vincent Van Pesch[26] · Celia Oreja-Guevara[27] · Anneke van der Walt[1] · Vilija G. Jokubaitis[1] Tomas Kalincik[28,29] · Helmut Butzkueven[1] on behalf of The MSBase Investigators



InRAD will enable robust, comparative health research

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A Pivotal Moment for a Unified Approach

- InRAD the **first & only international, sustainable registry solution** in AD
  - Foundation to overcome fragmentation when EMRs are not designed for research
  - InRAD enables value assessment and comparative health research
- We defined a **Minimum Data Set (MDS) and Extended Data Set (EDS)**, ensuring **standardised, high-quality data collection** across AD registries[1]
- We developed a data dictionary and common data model, providing a **blueprint for structured and harmonised data capture**, enabling seamless integration across diverse healthcare systems
- **The registry is about to launch**:
  - Pilot starting in **November 2025**
  - Wider international roll out from **January 2026**
  - Natural History study protocol in development
    - Motivating clinicians: High-quality data requires time and incentives
- **Joining InRAD means making a bigger impact** than any single centre could alone.
- EMA workshop on AD patient registries on 15th December

📌 InRAD **resources available** https://www.inradnetwork.org

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1. Perneczky et al. Real-world datasets for the International Registry for Alzheimer's Disease and Other Dementias (InRAD) and other registries: An international consensus, The Journal of Prevention of Alzheimer's Disease 2025 https://doi.org/10.1016/j.tjpad.2025.100096

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Thank you!

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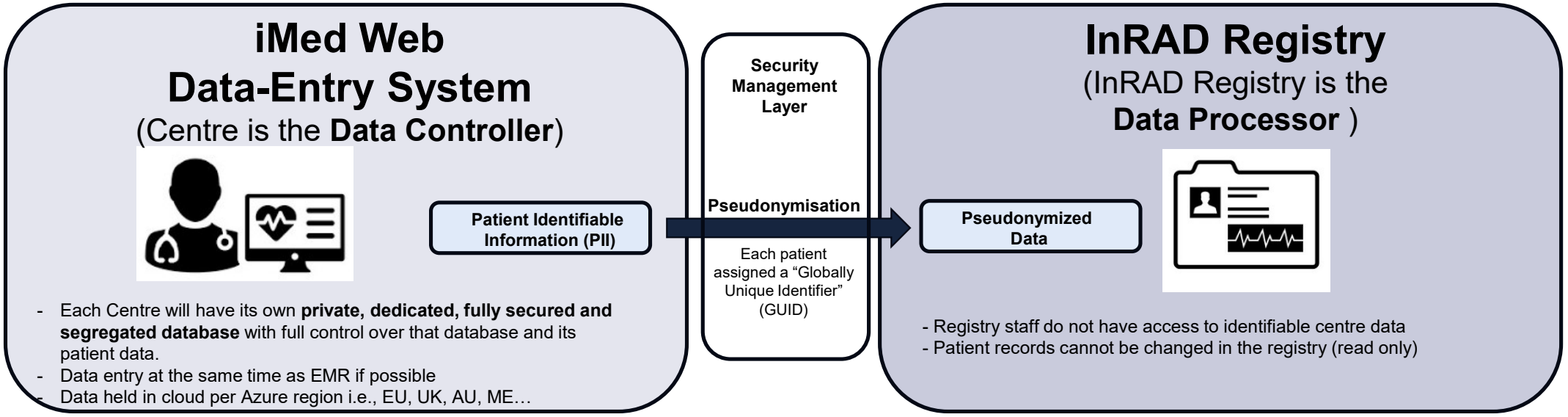
Data processing and flow



- The centre is the owner of all their data and can request to withdraw data from the Registry at any time
- Principal Investigators choose how their centre data is used and can opt-out of any investigator-initiated project requesting access to the global dataset

- InRAD Foundation runs the registry, provides the operational and administrative support to enable Investigators & SLG to conduct research analyses and studies by using the registry, support with biostatistical resources

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