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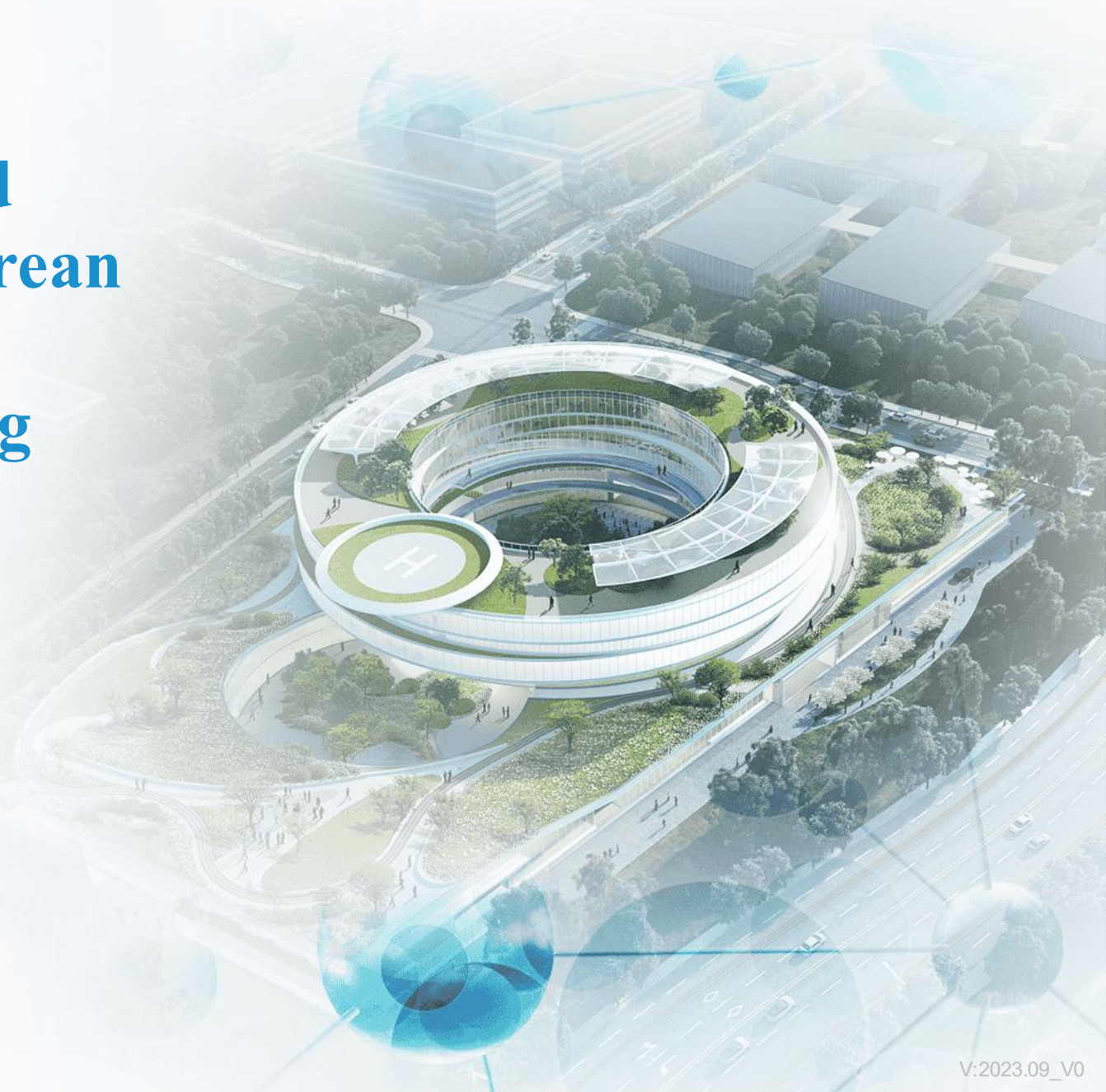
Annualized Relapse Rate and Clinical Profiles in South Korean Multiple Sclerosis Patients: A Sample Cohort Study Using Korean National Health Insurance Data



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Biography

Speaker

Jisuk Jo

Director of Statistics Department

- Ph.D. in Science/Biostatistics
- Over 20 years Data Management, Biostatistics and Bioinformatics in Samsung Medical Center, LSK Global PS and DreamCIS
  - Experience of various indications as Biostatistician and Data Management in Clinical Trials and PMS
  - Global Standard in Clinical Trials; CDISC – SDTM and ADaM
  - RWD/RWE; Clinical Data Analysis with EHR/EMR and Big Data Analysis with HIRA, NHIS
  - Translational research; Genetic; NGS, DEG, predicted model
- Volunteer of data standardization in Korea as a CDISC K3C member from 2025

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of DreamCIS.*

- *The author has no real or apparent conflicts of interest to report.*

Contents

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01

RWE/RWD

Paper RE01

Annualized Relapse Rate and Clinical Profiles in South Korean Multiple Sclerosis Patients: A Sample Cohort Study Using Korean National Health Insurance Data

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Jisuk Jo, DreamCIS Inc., Seoul, Korea

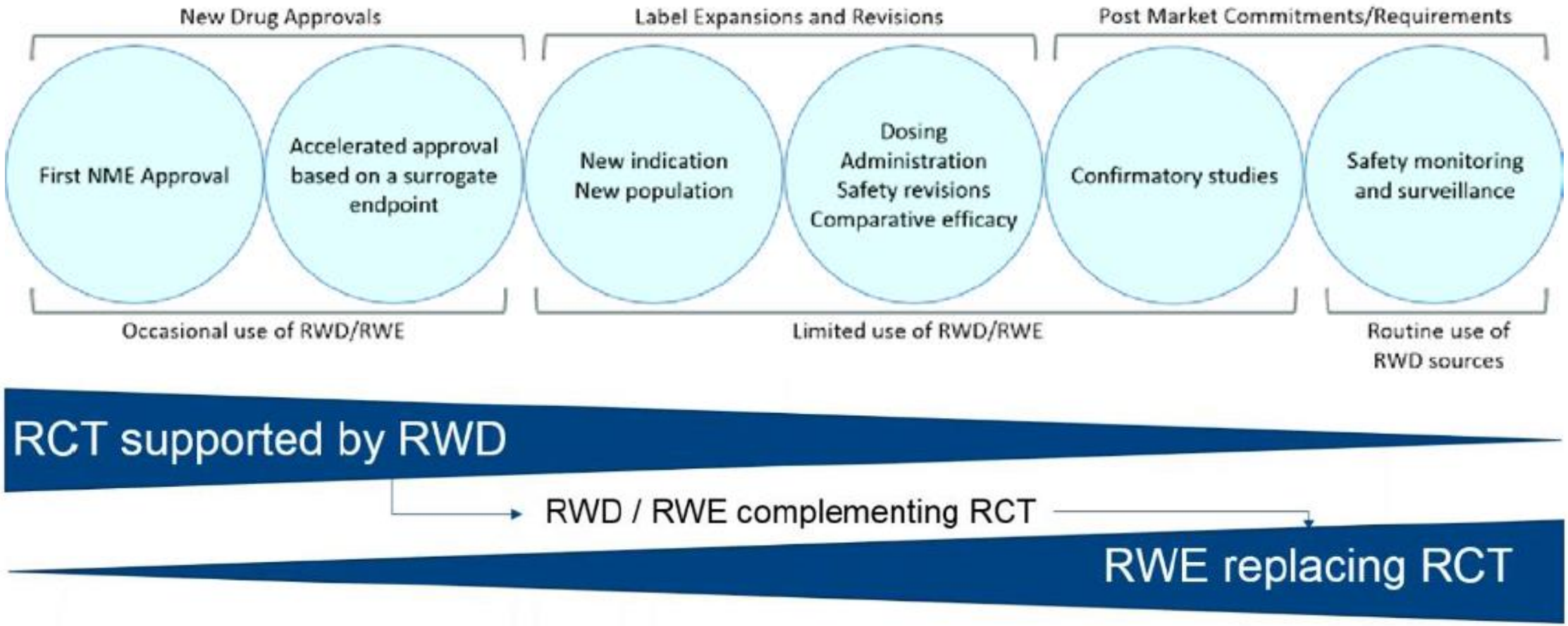
ABSTRACT

Background:

Multiple Sclerosis (MS) is a chronic, immune-mediated disorder of the central nervous system, with a globally increasing prevalence. This study aimed to explore the potential of Annualized Relapse Rate (ARR) as a predictor of disease course in Korean MS patients, using the National Health Insurance Service (NHIS) sample cohort data (2007-2019). Given the sample size, this study serves as an exploratory analysis to characterize relapse patterns in a Korean MS cohort. Additionally, we sought to generate Real-World Evidence (RWE) by analyzing the clinical characteristics and relapse risk factors among Korean MS patients.

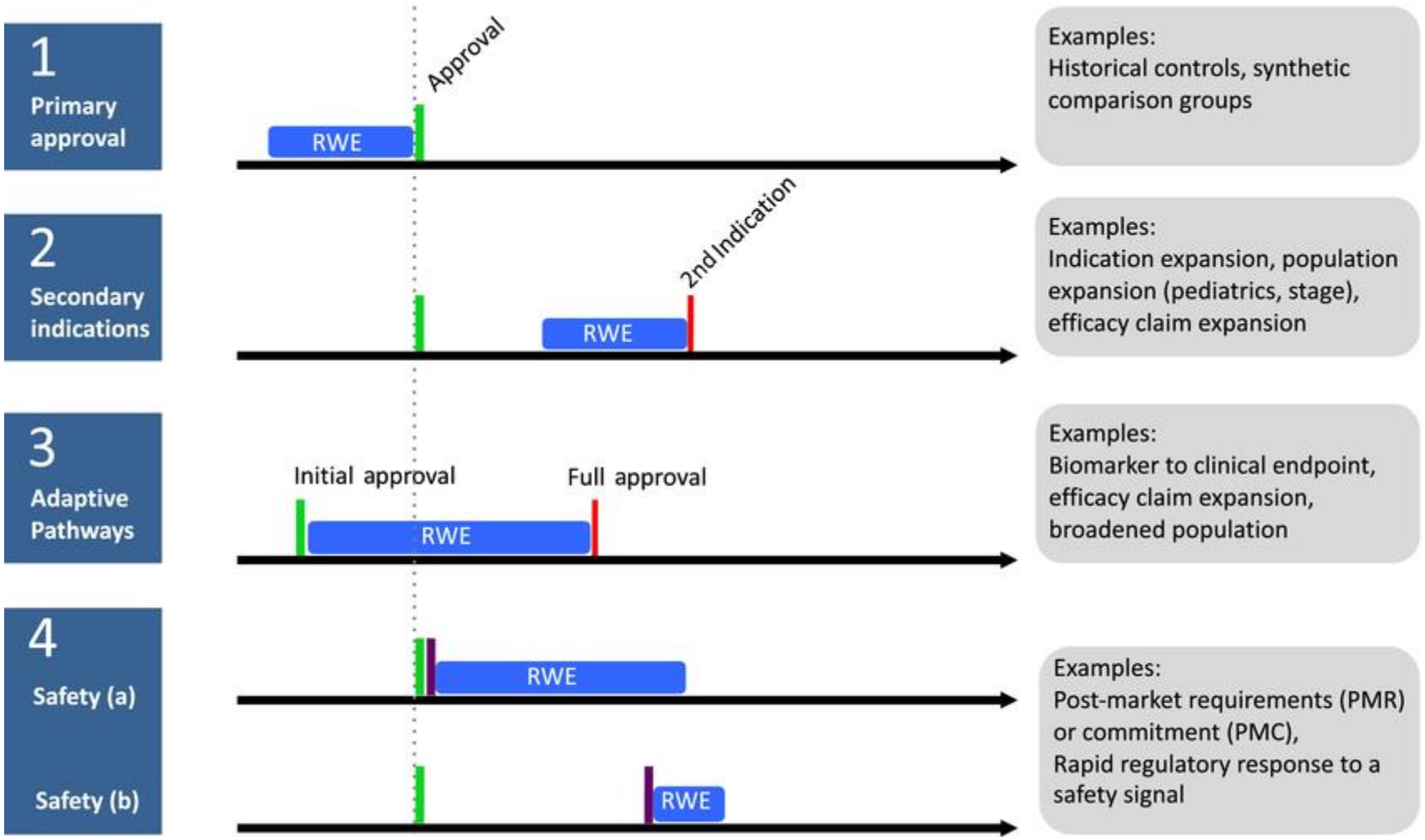
Keywords: Multiple sclerosis (MS), Annualized Relapse Rate (ARR), Real-World Evidence (RWE), National Health Insurance Service (NHIS), Ethnic Differences

Real-World Evidence (RWE)



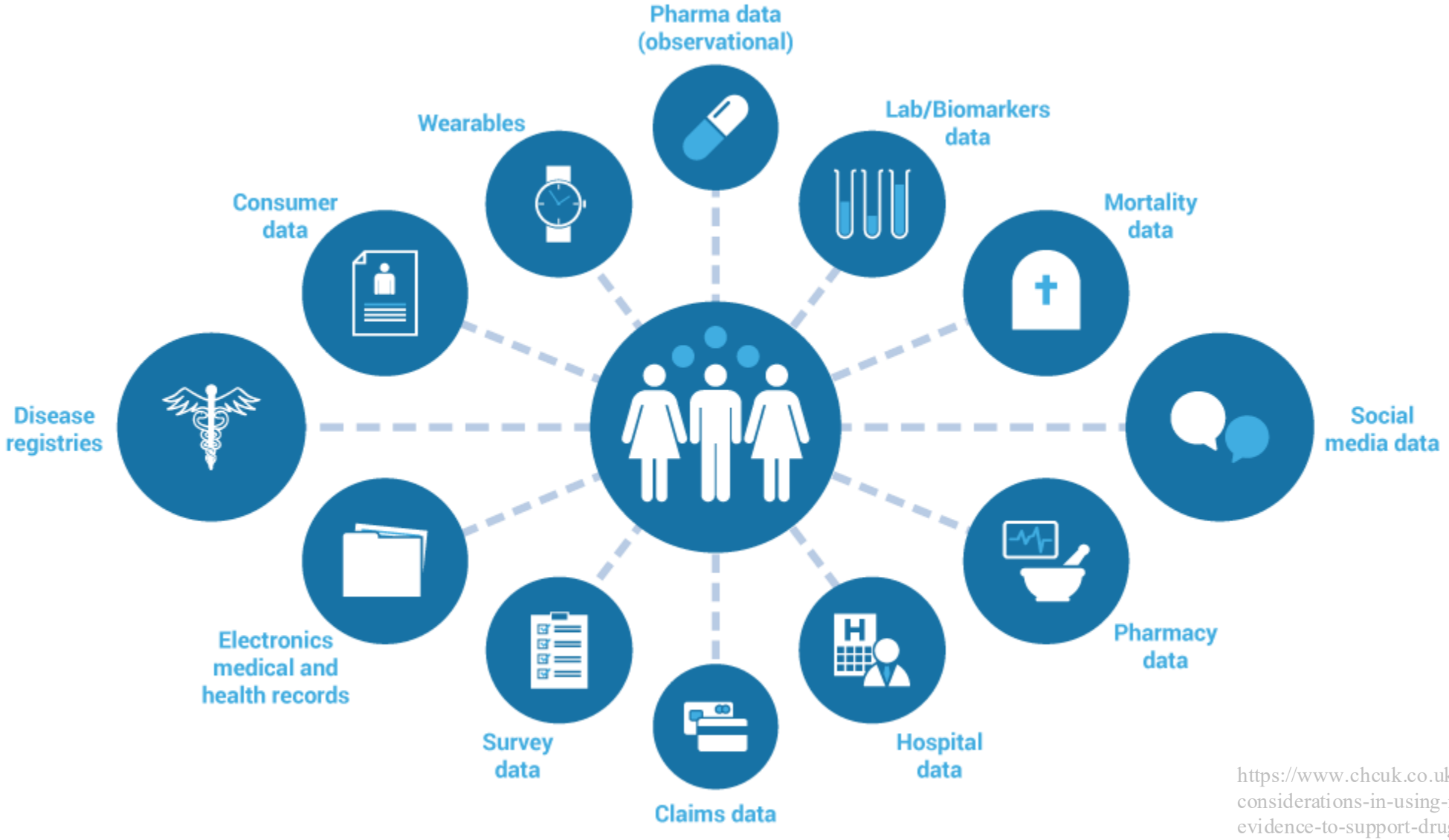
https://www.researchgate.net/figure/fig1_319650416 Source: TriNetX Summit Presentation (2019)

Real-World Evidence in Regulatory Decision Making



https://www.researchgate.net/figure/Real-world-evidence-RWE-in-regulatory-decision-making-key-use-cases_fig1_330355252

Real World Data (RWD)



https://www.chcuk.co.uk/china-key-considerations-in-using-real-world-evidence-to-support-drug-development/

Healthcare Big Data Platform – Dataset Provision Overview

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Providing Institution	Data Coverage Period	Dataset Description	Dataset Scale
Korea Disease Control and Prevention Agency (KDCA)	2007–2020	Korea National Health and Nutrition Examination Survey (KNHANES) – Air Pollution DB	Total 3 datasets, 965 variables
	2007–2022	Korea National Health and Nutrition Examination Survey (KNHANES) – Core DB	Total 16 datasets, 13,486 variables
	2013–2023	Tuberculosis Notification DB	Total 1 dataset, 16 variables
	2001–2013	KoGES (Korean Genome and Epidemiology Study)	Total 1 dataset, 34 variables
	2012–2023	Immunization Registry DB	Total 1 dataset, 8 variables
Statistics Korea	2012–2022	Cause of Death Statistics	Total 1 dataset, 7 variables
Korea Organ Donation Agency (KODA)	2012–2022	Donor Information, Transplant Recipient Information	Total 2 datasets, 210 variables
National Rehabilitation Center	2012–2022	Nursing Clinical Observation Records, Detailed Information for Medical Records	Total 5 datasets, 62 variables
Health Insurance Review & Assessment Service (HIRA)	2014–2023	Claims General Information, Medical Treatment Details, etc.	Total 4 datasets, 58 variables
National Cancer Center	1999–2021	Cancer Registry	Total 1 dataset, 7 variables
National Medical Center	2018–2021	Dementia Management Data	Total 11 datasets, 245 variables
National Health Insurance Service (NHIS)	2013–2022	Eligibility & Contribution, General Health Screening, etc.	Total 11 datasets, 548 variables
NHIS Ilsan Hospital	2012–2022	Patient Information, Diagnoses, Tests, Surgical Procedures, etc.	Total 7 datasets, 49 variables

https://www.aitimes.kr/news/articleView.html?idxno=30941

NHIS Big Data Offerings

Item	Sample Cohort DB	Customized Research DB
Definition	Standardized DB created by sampling high-demand data from nationwide NHIS data for policy/academic use	DB extracted, summarized, and processed from NHIS & Long-term care insurance data based on the applicant's research purpose
Number of Subjects	~1,000,000	Researcher-defined (custom)
Access Method	Remote server	On-site analysis center visit
Sensitive diagnoses	Masked	Masked (can be provided upon request)
Mortality information	Available (linked with Statistics Korea)	Available (linked with Statistics Korea)
Health screening info	Available	Available upon request
Rare diseases	Not provided	Conditionally available

NHIS 1M Sample Cohort: What's Inside (+ Mortality Linkage)

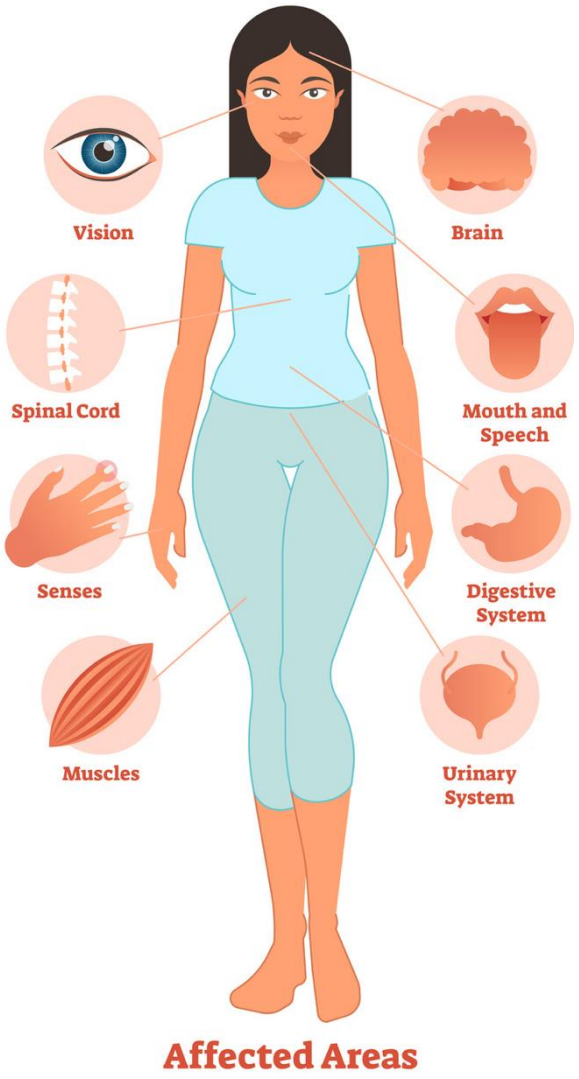
Eligibility & Premium DB	• DOB, sex, residence, eligibility status, immigration/travel history • Income (total/earned), etc. • National merit status, disability registration, etc.
Healthcare Utilization (Claims) DB	• Service statement: facility, diagnosis incl. primary/secondary, length of stay, etc • In-hospital treatments/procedures/surgeries, etc • Prescriptions: Over-the-counter prescription drugs, dose, days supplied, etc.
Health Screening DB	• General screening, life-transition screening, 5 major cancer screenings, etc • Questionnaires (lifestyle, family history, past history, etc) • Measured results
Nursing Care Facilities DB	• Nursing care facility status by type, establishment type, and region, as well as information on facilities, equipment, and personnel

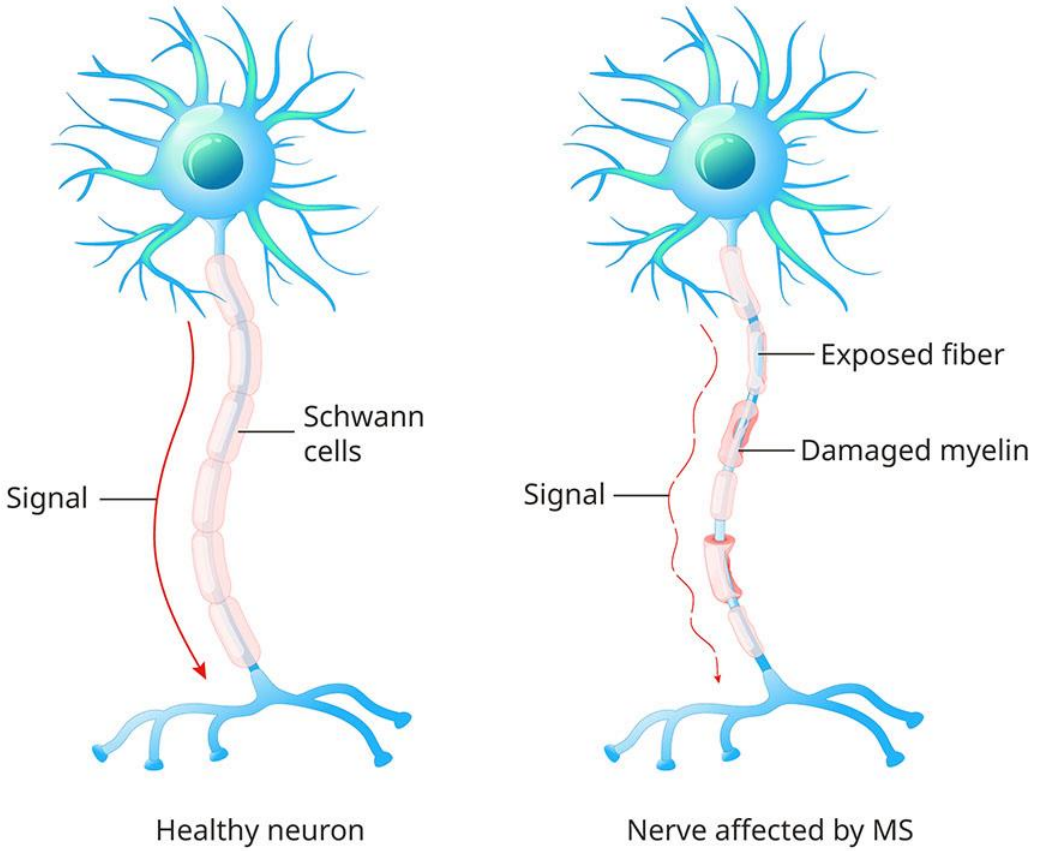
Linked to the Statistics Korea Cause of Death DB → Birth and death table

02

Multiple Sclerosis

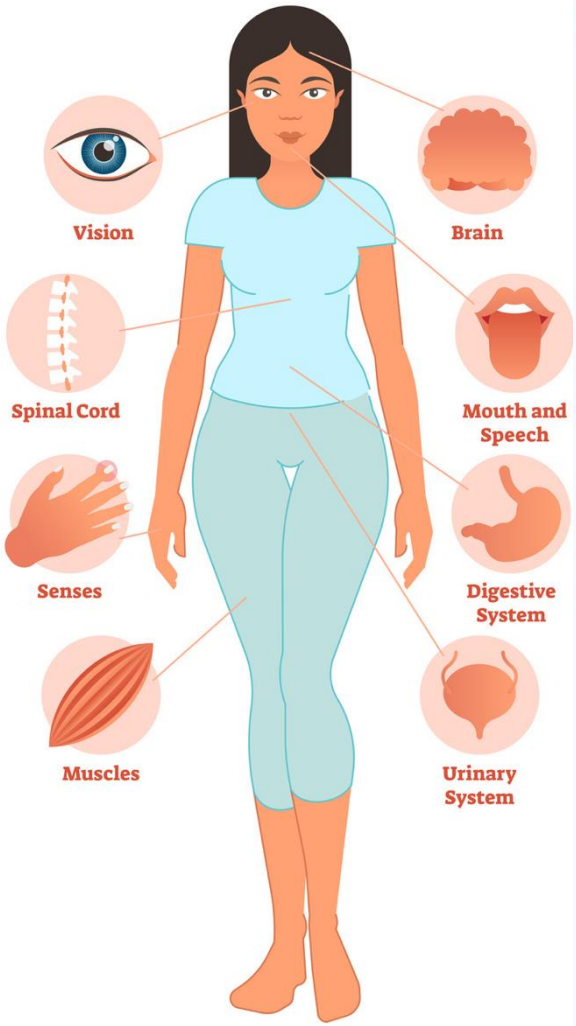
Multiple Sclerosis (MS)





 https://www.ohsu.edu/brain-institute/understanding-multiple-sclerosis?utm_source=chatgpt.com

Multiple Scler



Affected Areas

Muscle weakness

Numbness or tingling

Balance problems

Vision problems

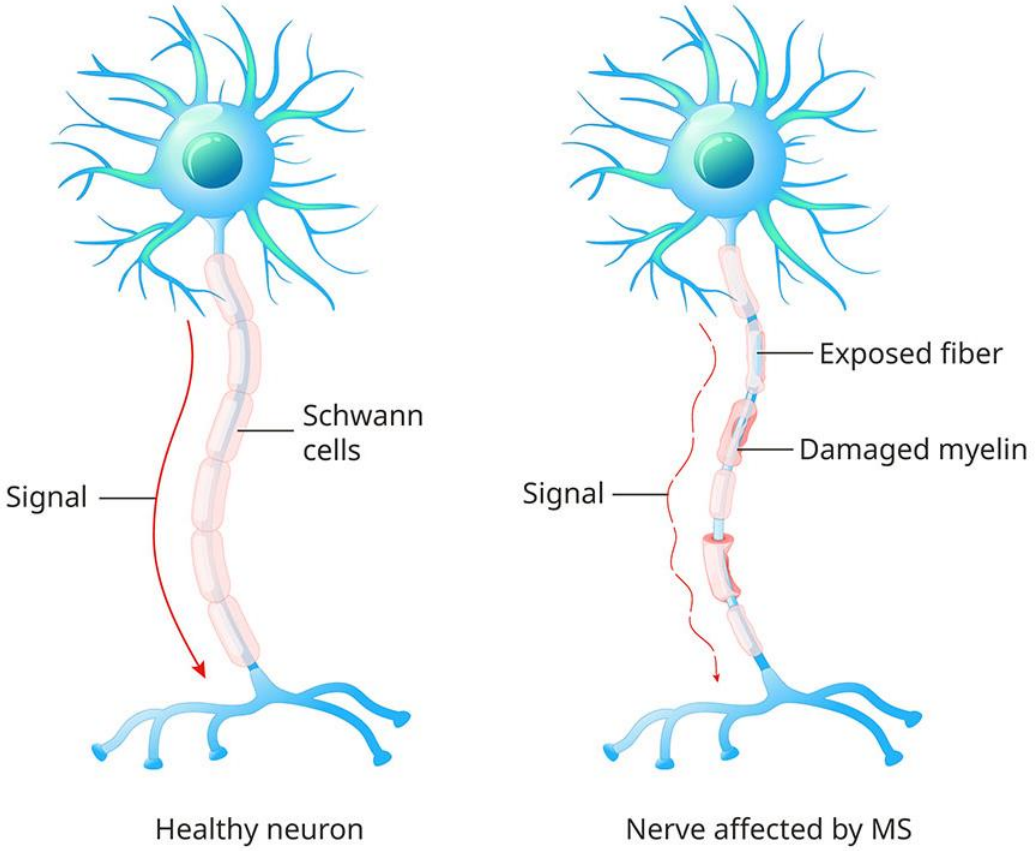
Tiredness

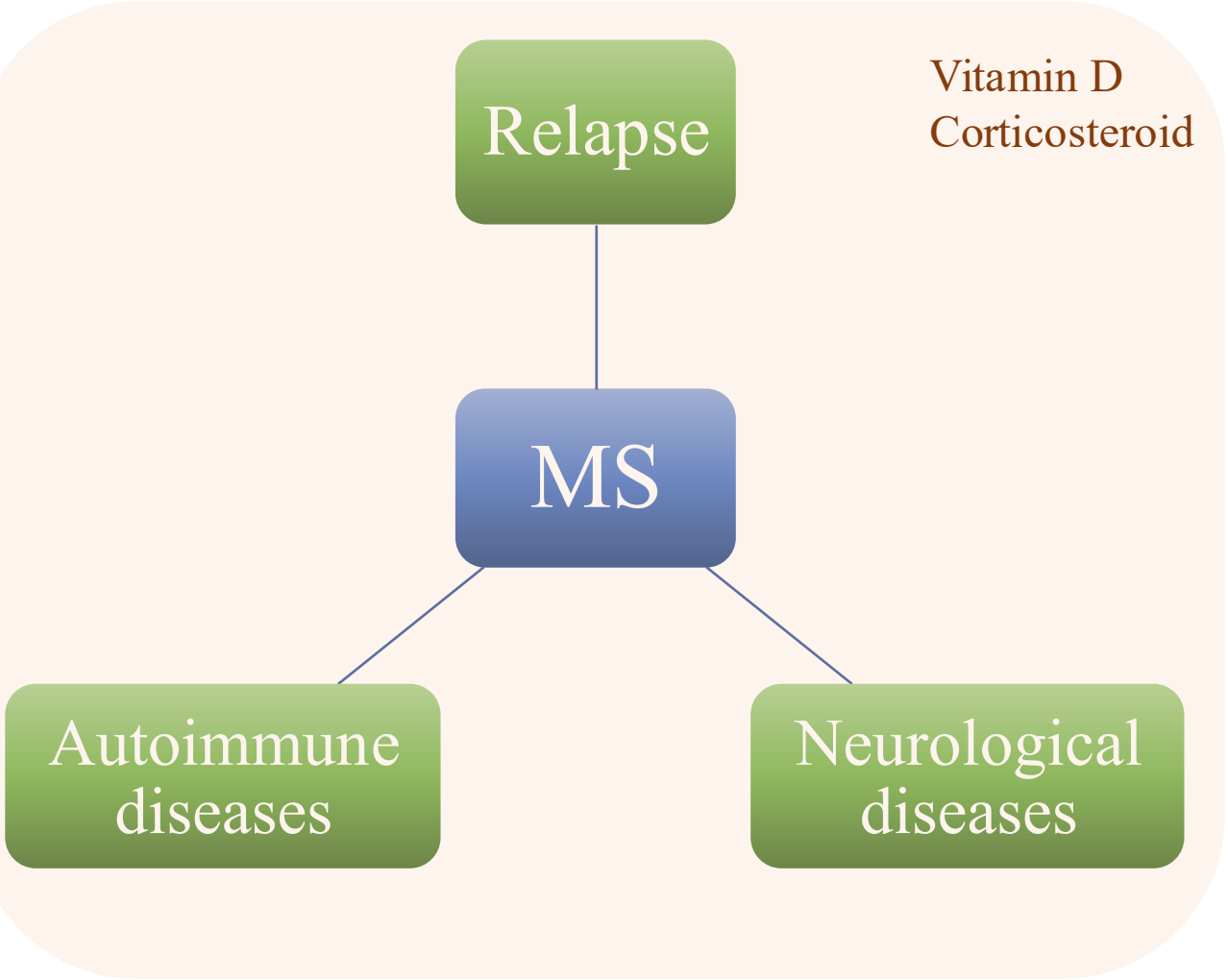
Stiffness or spasms

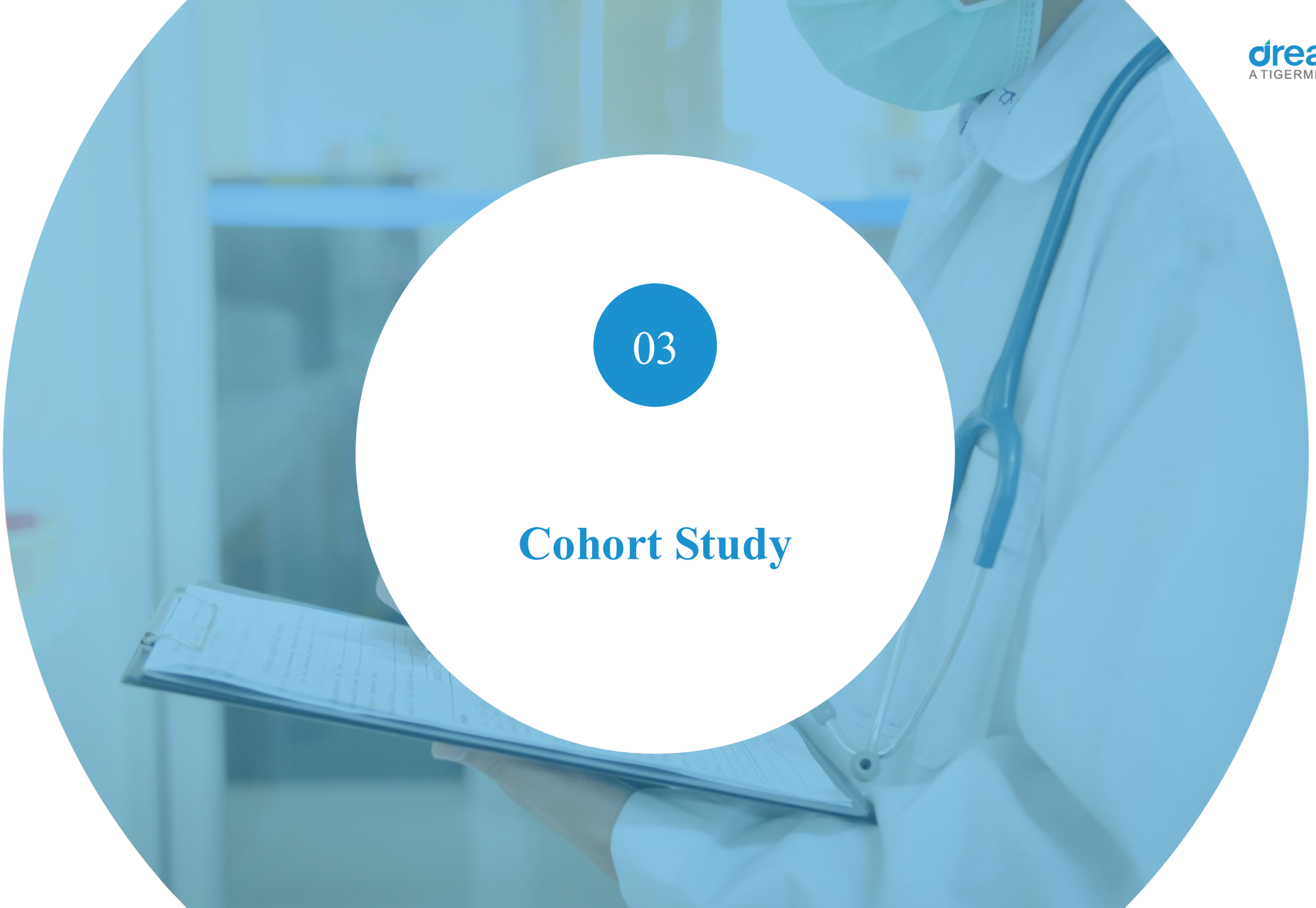
Bladder and bowel problems

Changes in mood and thinking

Multiple Sclerosis (MS)







03

Cohort Study

Background

❖ A study on PMS for multiple sclerosis (MS) was conducted to evaluate the effectiveness of annual relapse rate. (∵ Annual relapse rate is an important treatment criterion in patients with MS.)

- ✓ In PMS, the FU period for most enrolled patients is 1-2 years.
- ✓ Due to the short observation period, further clarification was requested

  → a report on the treatment period and endpoints in the usability study was prepared.
  - Average relapse rate is a time-varying variable, with a high probability of relapse at diagnosis but decreasing over time.
  - The study was found to have sufficient power to detect a significant reduction in relapses at a minimum of 1 year (AmyM. Lavery et al., 2014).
  - Although annual relapse rate should be assessed at 2 years, it is often also assessed at 1 year, and such results are considered an acceptable endpoint (Richard Nicholas et al., 2012).

➢ Using real-world data, we aimed to determine whether annual relapse rate differs according to treatment duration in Korean multiple sclerosis patients.

Operational Definition of the Study

- Multiple Sclerosis (MS)

  : Diagnosed with MS at least twice during the observation period (2009-2019)

  - Included: International Classification of Disease-Tenth Revision (ICD-10) codes for MS (G35)

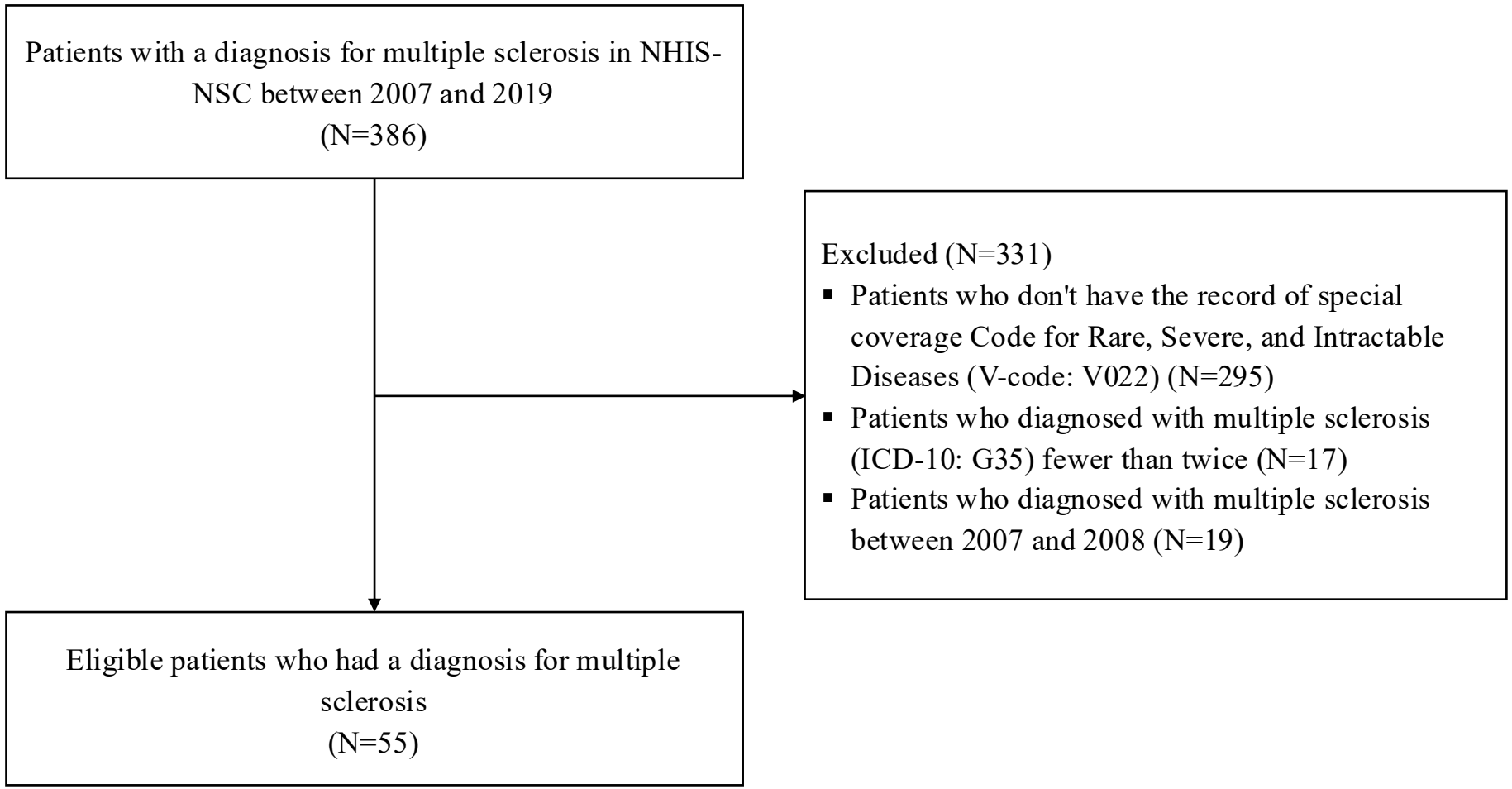
    + with a V-code (V022), which is designated for tracking patients with RID

  - Excluded: no record of the V-code (V022) and those diagnosed with MS fewer than twice with the V-code during the observation period

    + MS patients diagnosed with MS in 2007 or 2008

RID = rare, intractable diseases

Flow Chart of the Study Population



Baseline Characteristics of MS Patients

	MS patients (n=55)
Age, mean ± SD (year)	45.20 ± 16.17
Age group, n (%)	
< 20 years	2 (3.64%)
20 ~ 39 years	20 (36.36%)
40 ~ 59 years	24 (43.64%)
≥ 60 years	9 (16.36%)
Sex, n (%)	
Male	17 (30.91%)
Female	38 (69.09%)
BMI, n (%)	
Underweight (< 18.5)	3 (5.45%)
Normal bodyweight (18.5 to < 23)	8 (14.55%)
Overweight (≥23)	10 (18.18%)
Missing/Unknown	34 (61.82%)
Medication, n (%)	
Vitamin D	4 (7.27%)
Corticosteroid	40 (72.73%)
Overall health status	
No. of outpatient visits, mean ± SD	7.71 ± 6.23
No. of Emergency room (ER) visits, mean ± SD	1.07 ± 1.49
No. of prescription of steroids, mean ± SD	2.04 ± 2.29
No. of hospitalization, mean ± SD	2.20 ± 3.45
Duration of hospitalization, median (Q1 - Q3)	21 (8 – 119)

Table 2. History of Other Autoimmune Disease of MS Patients

	MS patients (n=55)
Autoimmune Disease (n, %)	11 (20.00%)
Rheumatoid Arthritis	6 (10.71%)
Narcolepsy	3 (5.45%)
Systemic sclerosis	3 (5.45%)
Myasthenia Gravis	2 (3.57%)
Antiphospholipid Syndrome	1 (1.82%)
Chronic Inflammatory Demyelinating Polyneuropathy	1 (1.82%)

Table 3. History of Disease Related to Symptoms of MS Patients

	MS patients (n=55)
Myelitis	11 (20.00%)
Neuromyelitis Optica Spectrum Disorder (NMOSD)	5 (9.09%)
Sensory syndrome	3 (5.45%)
Visual syndrome	3 (5.45%)
Motor syndrome	1 (1.82%)

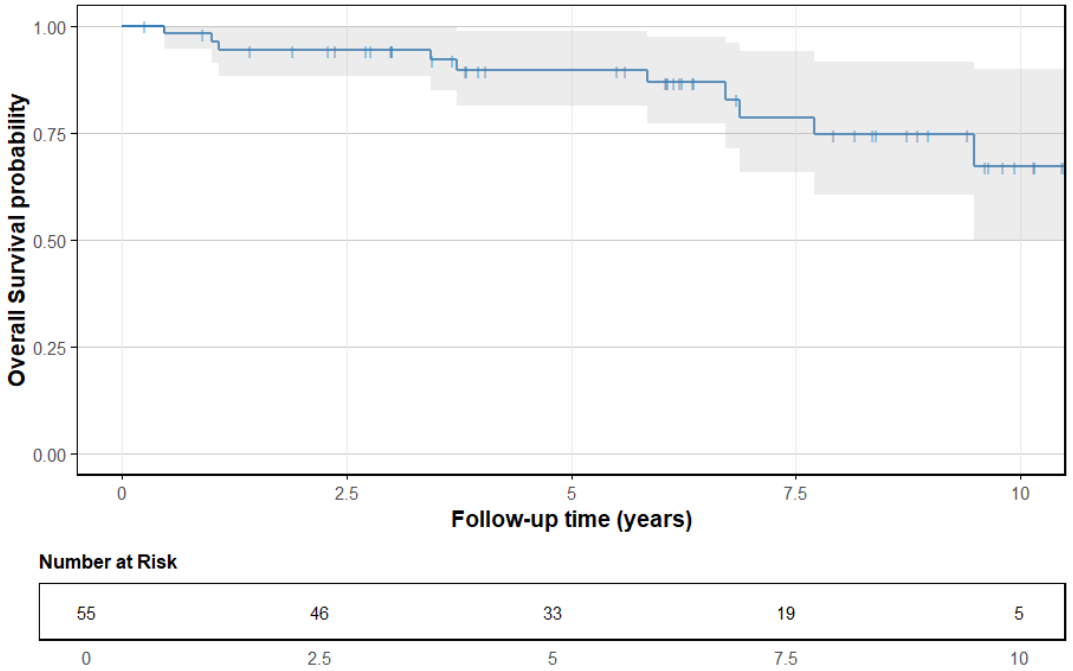


Figure 2. Kaplan-Meier Curve of Overall Survival in MS Patients

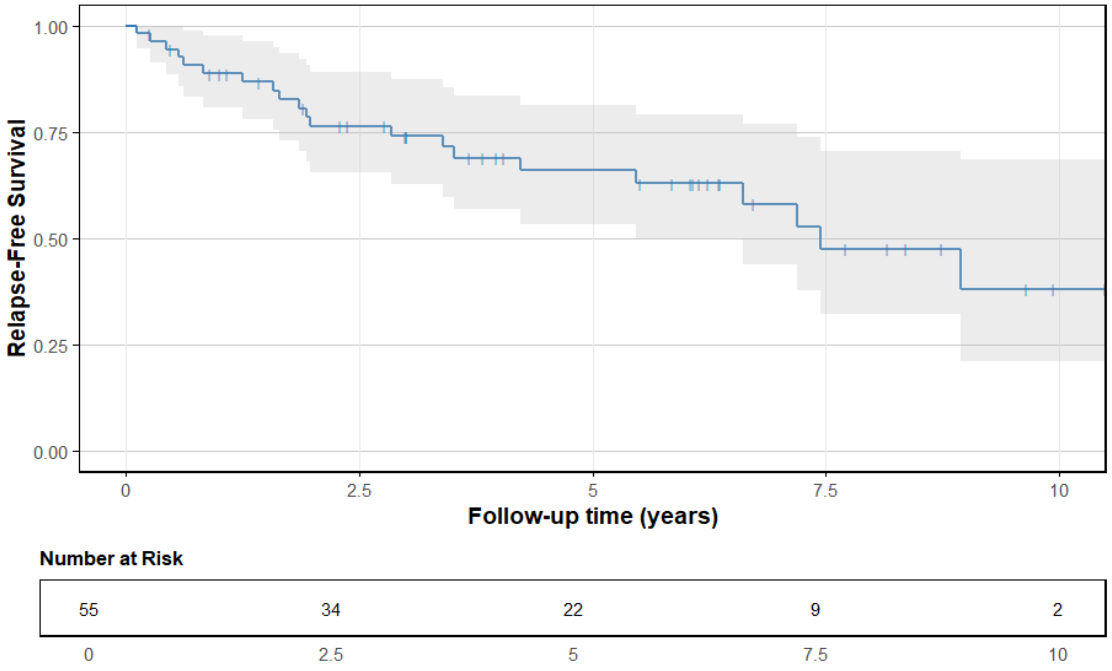


Figure 3. Kaplan-Meier Curve of Relapse-Free Survival in MS Patients

Annualized Relapse Rate (ARR)

- Relapse
  - Using hospitalization records
  - Same relapse episode = 1 relapse = multiple hospitalization claims occurring within a 30-day window
  - Distinct relapse events = N relapse = hospitalizations separated by ≥30 days

- The general formula of ARR is expressed as follows: $$ARR = \sum_i \left(\frac{r_i}{t_i} \times \frac{t_i}{T} \right) = \frac{\sum_i r_i}{\sum_i t_i}$$

  , where the subscript i represents each individual, ri is the number of relapses during follow-up in each individual, ti is the length of follow-up in each individual, and T is the total sum of follow-up periods within the cohort

- The standard method for calculating the crude ARR in a study cohort is the person-years method as follows:

$$ARR = \frac{Total\ number\ of\ relapses}{Total\ person\ time\ (in\ years)\ at\ risk\ of\ relapse}$$

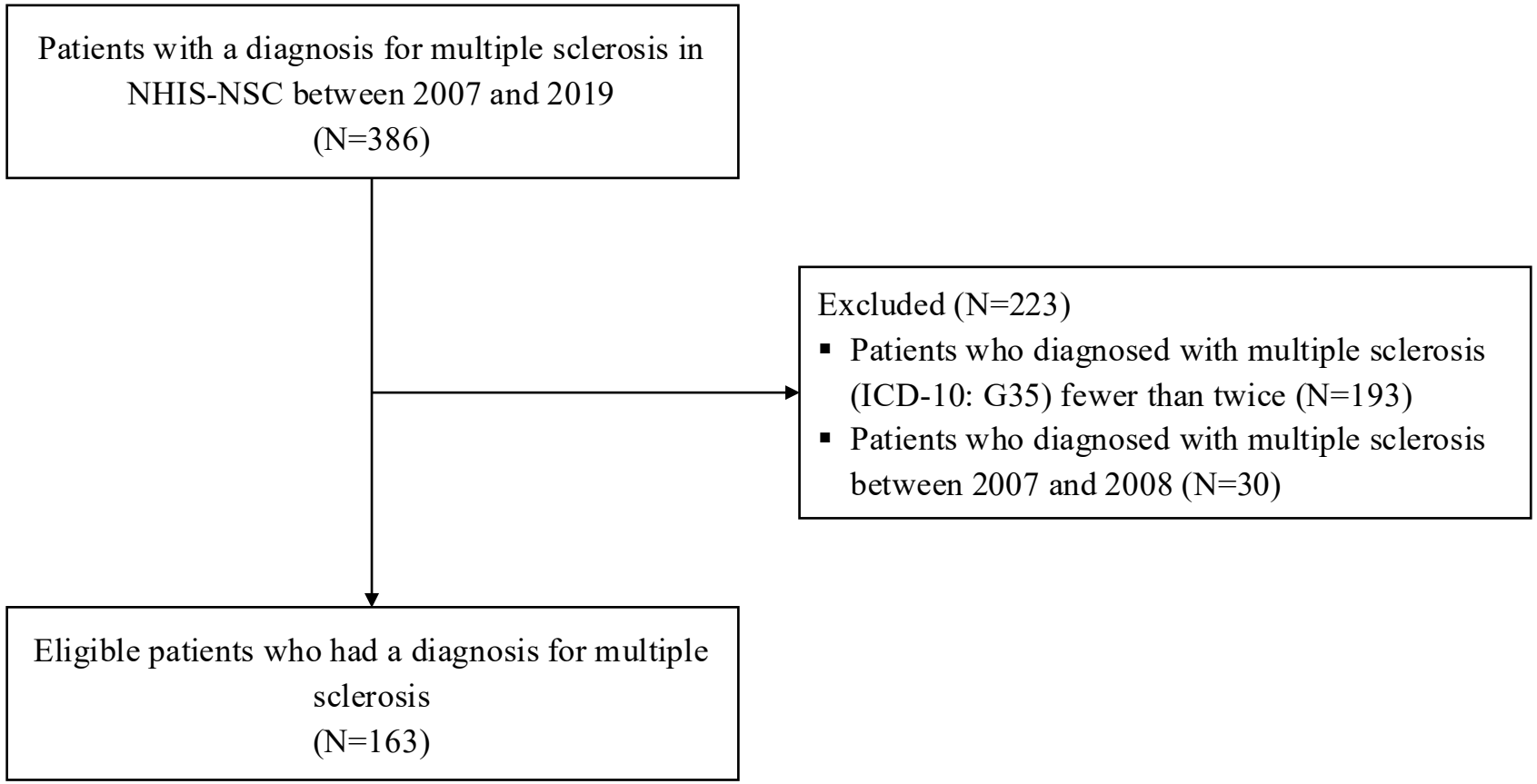
  - If individual follow-up periods vary, each participant's time at risk is summed to find the total.
  - For each patient, follow-up time was calculated in days from the index date to the last observed claim date or death, whichever came first, and converted to PY by dividing by 365.25

Akaishi T, Ishii T, Aoki M, Nakashima I. Calculating and Comparing the Annualized Relapse Rate and Estimating the Confidence Interval in Relapsing Neurological Diseases. Frontiers in neurology. 2022;13:875456.

Table 4. Annualized Relapse Rate of MS Patients according to Follow-up duration after Diagnosis

Follow-up duration category (since diagnosis)	No. of relapse	No. of patients	Sum of PYs (years)	Crude ARR (95% CI)
≤1 year since first diagnosis	7	6	53.62	0.13 (0.05, 0.27)
≤2 years since first diagnosis	16	12	103.04	0.16 (0.09, 0.25)
≤3 years since first diagnosis	23	13	149.20	0.15 (0.10, 0.23)
≤4 years since first diagnosis	28	15	188.16	0.15 (0.10, 0.22)
≤5 years since first diagnosis	30	16	221.22	0.14 (0.09, 0.19)
≤6 years since first diagnosis	33	17	253.18	0.13 (0.09, 0.18)
≤7 years since first diagnosis	35	18	276.12	0.13 (0.09, 0.18)
Total	39	21	320.08	0.12 (0.09, 0.17)

Flow Chart of the Study Population (Sensitivity Analysis)



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Total	39	21	320.08	0.12 (0.09, 0.17)

Table 5. ARR of MS according to Follow-up duration after Diagnosis (Sensitivity Analysis: Redefined Cohort)

Follow-up duration category (since diagnosis)	No. of relapse	No. of patients	Sum of PYs (years)	Crude ARR (95% CI)
≤1 year since first diagnosis	14	10	158.09	0.09 (0.05, 0.15)
≤2 years since first diagnosis	25	17	305.17	0.08 (0.05, 0.12)
≤3 years since first diagnosis	32	18	436.13	0.07 (0.05, 0.10)
≤4 years since first diagnosis	38	21	549.02	0.07 (0.05, 0.10)
≤5 years since first diagnosis	40	22	642.54	0.06 (0.04, 0.08)
≤6 years since first diagnosis	43	23	723.26	0.06 (0.04, 0.08)
≤7 years since first diagnosis	46	24	778.13	0.06 (0.04, 0.08)
Total	50	27	862.68	0.06 (0.04, 0.08)

Conclusion

- This exploratory study of a Korean MS sample cohort suggests that hospitalization-requiring relapses are most frequent within the first two years after diagnosis and decline thereafter

Strengths

- The first real-world study exploring MS relapse using a large-scale, nationwide health insurance database in Korea
- By leveraging comprehensive claims data, our study provides valuable epidemiologic insights into relapse pattern in the Korean MS population

Limitations

- Relapse was defined according to hospitalization records rather than comprehensive clinical criteria
- Relevant clinical variables was not available in our database and the small sample size – limitation of the generalizability

T h a n k Y o u

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