Developing a Case Identification Algorithm for Myasthenia Gravis in Real-World Evidence Databases: A Framework for Rare Disease Research

RWD261

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INTRODUCTION

Accurate case identification is a critical challenge in real-world evidence (RWE) studies of rare diseases. **Myasthenia gravis** (MG) exemplifies these challenges:

- MG is a rare autoimmune neuromuscular disorder characterised by fluctuating muscle weakness and fatigue.[1]
- **Diagnosis is frequently delayed**, with a median lag of up to two years due to mimicking conditions such as thyroid ophthalmopathy, oculopharyngeal muscular dystrophy, and chronic external ophthalmoplegia.[2]
- Ocular symptoms are the most common MG presentation (~50% of patients), but have many differential diagnoses (e.g., chronic external ophthalmoplegia, thyroid ophthalmopathy, oculopharyngeal muscular dystrophy).[3]
- RNS sensitivity: 75-80% in generalised MG, >90% in myasthenic crisis, but only 15-45% in ocular MG. Reliance on RNS benchmarks **biases case capture toward more severe MG**, underestimating ocular MG and associated healthcare utilisation.[4]

To overcome these limitations, we developed a multi-component algorithm designed to identify MG patients in the National Health Data Hub (NHDH) dataset. **Although tailored to MG, this methodology illustrates a generalizable framework for identifying rare disease cohorts in large administrative datasets**.

METHOD

Data Source

The NHDH is a comprehensive, linked national dataset capturing:

- Outpatient visits and diagnostic testing.
- Inpatient admissions and procedures.
- Pharmaceutical Benefits Scheme (PBS) and Repatriation PBS dispensing.
- Emergency department presentations.
- Mortality records.

Algorithm Development

Co-designed with two MG specialists and a pharmacoepidemiologist to integrate clinical reasoning with pharmacoepidemiological methods.

Key principles:

- Combine diagnostic codes, treatment dispensing patterns, procedural data, and diagnostic testing records.
- Address limitations of any single data source by triangulating evidence.
- Align with known MG epidemiology to ensure plausible cohort size.

OBJECTIVE

1. Develop a **reproducible algorithm** that balances sensitivity (capturing atypical or ocular MG) and specificity (excluding mimicking disorders).
2. Provide a **transparent methodology** applicable to other **rare diseases in RWE research.**

RESULTS

The final algorithm defines MG cases as patients meeting **any one** of five inclusion rules:

A — Prolonged pyridostigmine use

- ≥3 months of continuous pyridostigmine dispensing.
- Exclusion: concurrent use of fludrocortisone or propranolol (to avoid inclusion of autonomic disorders).

B — Therapeutic thymectomy

- Presence of a thymectomy procedure code, highly specific to MG management.

C — Combined treatment and diagnostic evidence

- At least one pyridostigmine prescription.
- An acetylcholine receptor (AChR) antibody test within 12 months.
- **Plus**, subsequent treatment with prednisone, prednisolone, azathioprine, methotrexate, tacrolimus, rituximab, IVIg, or PLEX.

D — Repeated diagnostic coding

- ≥2 hospital or emergency department encounters, at least three months apart, coded with ICD-10-AM G70.0 (MG).

E — Hybrid evidence rule

- At least one MG diagnostic code and fulfilment of ≥1 of criteria 1–3.

SIGNIFICANCE

- This algorithm provides more accurate case identification than ICD coding alone, particularly for patients with atypical or ocular presentations.
- It reduces the risk of bias introduced by diagnostic delays or incomplete coding.
- The framework is transferable to other rare conditions where low prevalence and coding limitations hinder valid cohort identification.

CONCLUSIONS

The proposed algorithm demonstrates a methodological advance in case identification for MG within administrative health datasets.

- It integrates clinical expertise, pharmaceutical use patterns, diagnostic testing, and procedural data.
- This provides a foundation for reproducible rare disease research in real-world data.
- This approach ensures more accurate estimation of HCRU and costs, while offering a generalizable framework for other rare disease studies.

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