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KEY TAKEAWAY:

- This review identifies SNCA rs11931074 as a shared genetic signal across East Asian Parkinson’s disease cohort.

INTRODUCTION

- Parkinson's disease (PD) is a progressive neurodegenerative disorder with multifactorial etiology and polygenic risk factors.¹
- Elucidating the genetic architecture of PD may improve early risk stratification, clarify disease-associated biological pathways, and support prioritization of therapeutic targets.²
- Despite extensive genetic association literature, evidence linking PD-associated variants to actionable therapeutic targets remains fragmented and inconsistent across populations.

OBJECTIVES

- To synthesize high-quality evidence on single nucleotide polymorphisms (SNP) and genetic polymorphisms associated with PD.
- To identify recurrent SNP-gene associations and shared genetic signals across ethnic populations with potential relevance for genetic risk stratification and target prioritization.

METHODS

- This systematic review was prospectively registered with PROSPERO (ID: CRD42019127482)

Search Strategy

- A comprehensive Boolean search using MeSH terms and free-text keywords related to PD and genetic polymorphisms was conducted across PubMed, Cochrane Library, ProQuest, Europe PMC, HuGE Navigator, EMBASE, Ovid, Web of Science, and grey literature sources.
- Databases were searched from inception to December 2021, with no date or language restrictions.

Eligibility Criteria

- Human case-control studies were included if they evaluated genetic polymorphisms associated with PD, enrolled clinically diagnosed PD cases with appropriate controls, and reported extractable SNP, genotype, allele frequency, or association data.
- Reviews, meta-analyses, editorials, letters, case reports, conference abstracts, duplicate datasets, studies without controls, and studies lacking extractable genetic data were excluded.

Quality Appraisal

- Selected studies were assessed in two steps:
 - Newcastle-Ottawa Scale: studies with scores >6 (out of 8) were retained.
 - Q-Genie tool: studies with scores >35 were included.

Data Extraction

- Extracted variables included study characteristics, population details, diagnostic criteria, SNP and gene information, genotype or allele frequencies, association estimates, and Hardy-Weinberg equilibrium status where available.

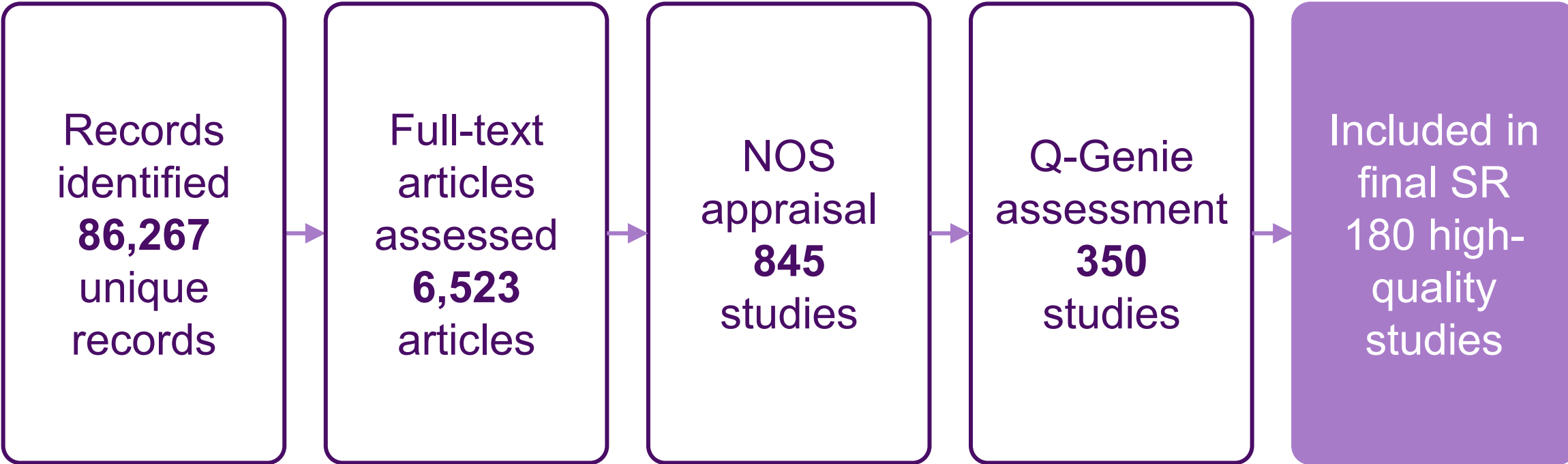
Evidence Synthesis

- SNPs were mapped to corresponding gene loci and stratified by ethnic population. Shared and population-specific signals were then evaluated, including intersection analysis across major East Asian cohorts.

RESULTS

- A systematic search across major databases identified 86,267 unique records. The study selection and quality appraisal process is summarized in **Figure 1**. The final evidence synthesis encompassed 39 distinct ethnic populations, evaluating 812 unique SNPs mapped to 345 gene loci.

Figure 1. PRISMA flowchart

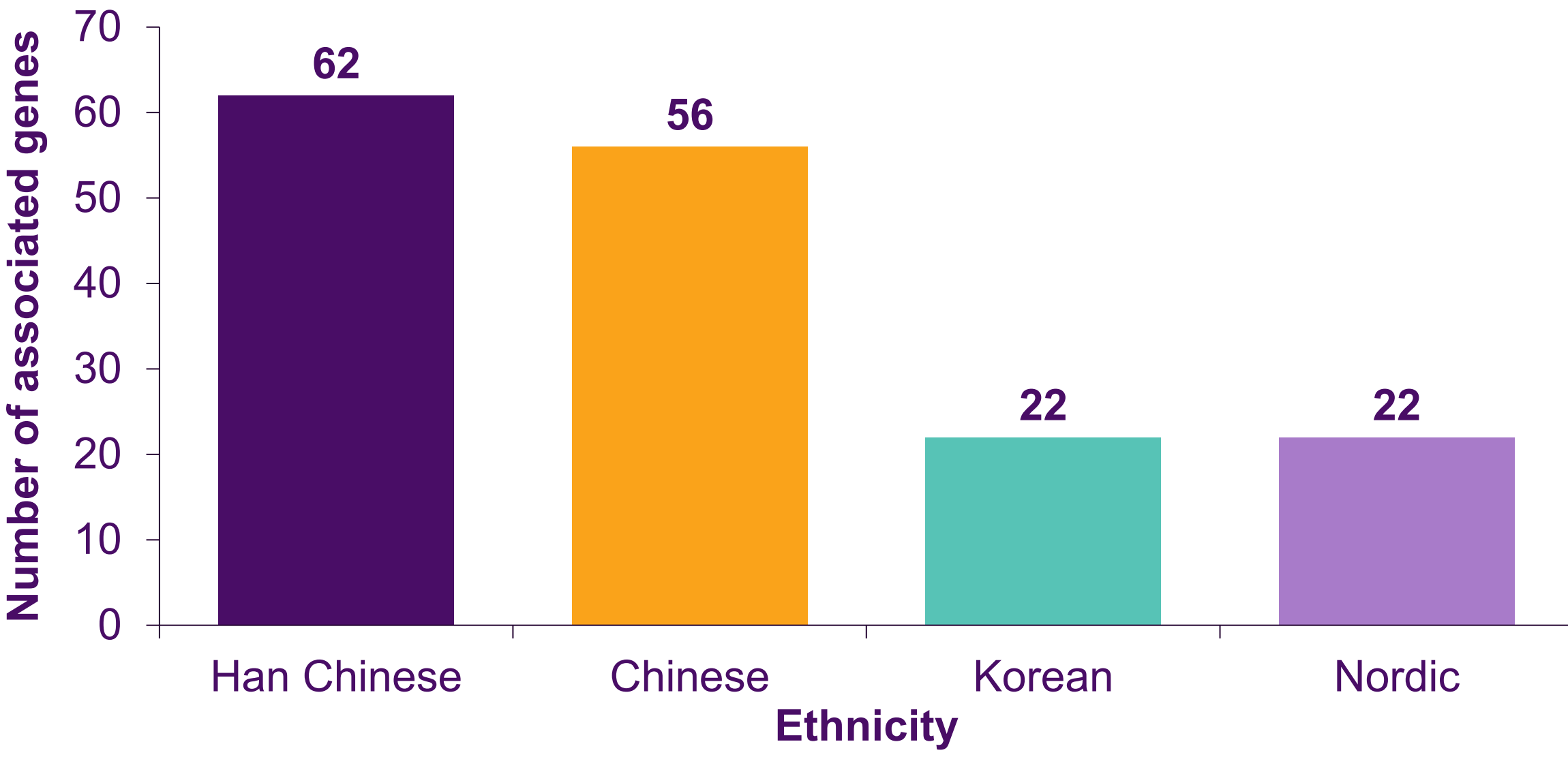


NOS, Newcastle-Ottawa Scale; PD, Parkinson's disease; Q-Genie, quality of genetic association studies; SR, systematic review.

Population-Level Evidence Base

- Gene association patterns varied across ethnic populations, as summarized in **Figure 2**.

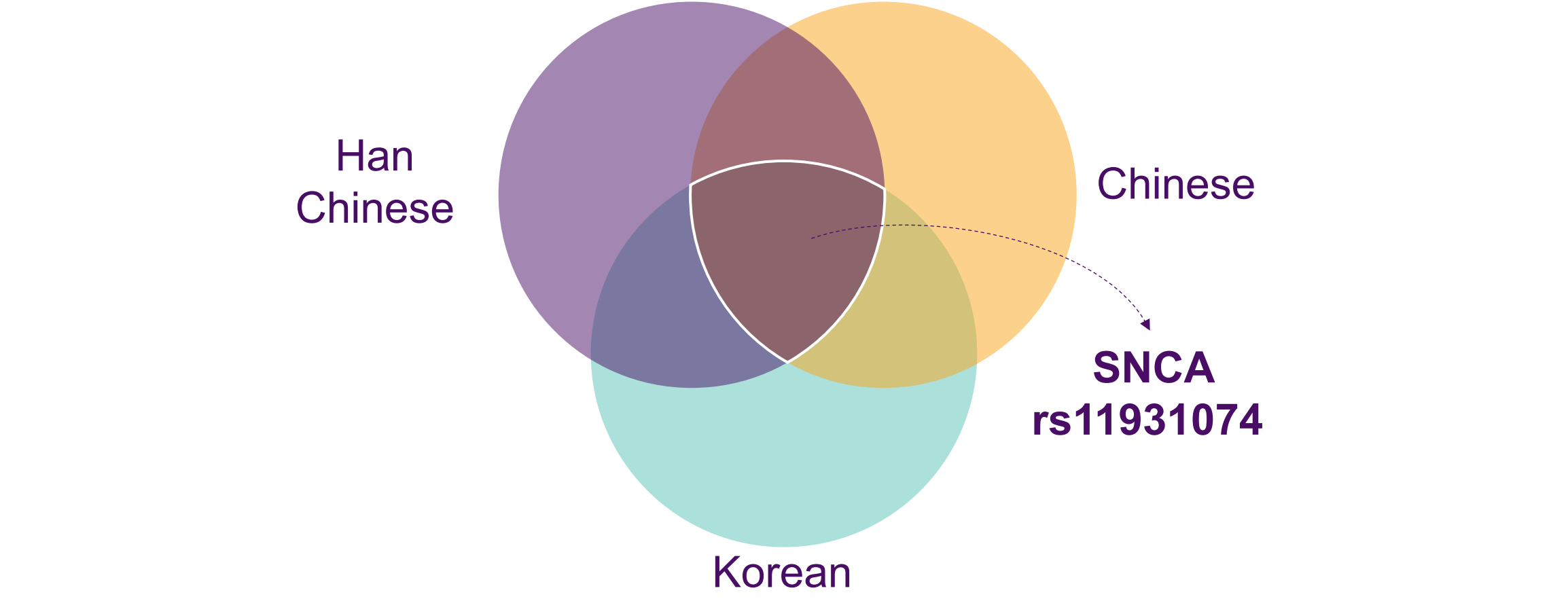
Figure 2. Ethnic populations with the highest frequency of gene associations



Key Genetic Findings

- Intersection analysis identified SNCA rs11931074 as a shared risk signal across East Asian cohorts, as shown in **Figure 3**.

Figure 3. Shared risk marker across East Asian cohorts



INTERPRETATION AND IMPLICATIONS

- The identification of an SNCA-linked signal is biologically plausible given the central role of alpha-synuclein in PD pathogenesis.
- The predominance of East Asian datasets indicates a population imbalance in the available genetic association evidence.
- Ethnicity-stratified SNP-gene mapping may help prioritize variants for replication and functional validation.

CONCLUSIONS

- This systematic review consolidated high-quality genetic association evidence from 180 studies, covering 39 ethnic populations, 812 SNPs, and 345 gene loci.
- SNCA rs11931074 emerged as a recurrent shared genetic signal across East Asian cohorts, supporting its relevance for further validation.
- The predominance of Han Chinese and Chinese datasets indicates a major population imbalance in the current PD genetics evidence base.
- Greater multi-ethnic representation, independent replication, and functional validation are needed to improve the generalizability and translational value of PD genetic findings.

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CONFLICTS OF INTEREST

None