

Probiotics, Omega-3, Glucosamine, And Inflammation: Cross-Sectional Associations With IL-6 In The Compass-ND Cohort

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INTRODUCTION

Background : Chronic low-grade inflammation is associated with aging and cognitive decline, and interleukin-6 (IL-6) is a widely studied circulating inflammatory marker. ^{1, 2}

Aim : This study examined whether current omega-3, glucosamine, or probiotic use was associated with IL-6 in the COMPASS-ND cohort.

METHODS

Design and participants : Cross-sectional analysis of baseline COMPASS-ND data collected across 31 Canadian sites. All available diagnostic groups were included. Of 1,010 participants with supplement records, 875 had complete IL-6, age, and sex data.

Variable	Definition
Supplement use	Omega-3, glucosamine, or probiotic use identified from medication records; each examined separately as user vs non-user
IL-6	Measured using the Elecsys® IL-6 assay on a cobas e platform
Covariates	Age and sex

Data Processing & Analysis : IL-6 was bounded at 1.5–20 pg/mL and log-transformed for regression. Medications/supplements with plausible anti-inflammatory relevance and ≥40 users in the full dataset underwent initial user-versus-non-user Welch’s t-test comparisons; after excluding missing IL-6, probiotics had 38 users. Omega-3, probiotics, and glucosamine were carried forward to age- and sex-adjusted HC3 models (two-sided α = .05).

RESULTS

Key finding:

In exploratory age- and sex-adjusted models, probiotic use was associated with lower IL-6 (p = .030); no statistically significant associations were observed for omega-3 or glucosamine.

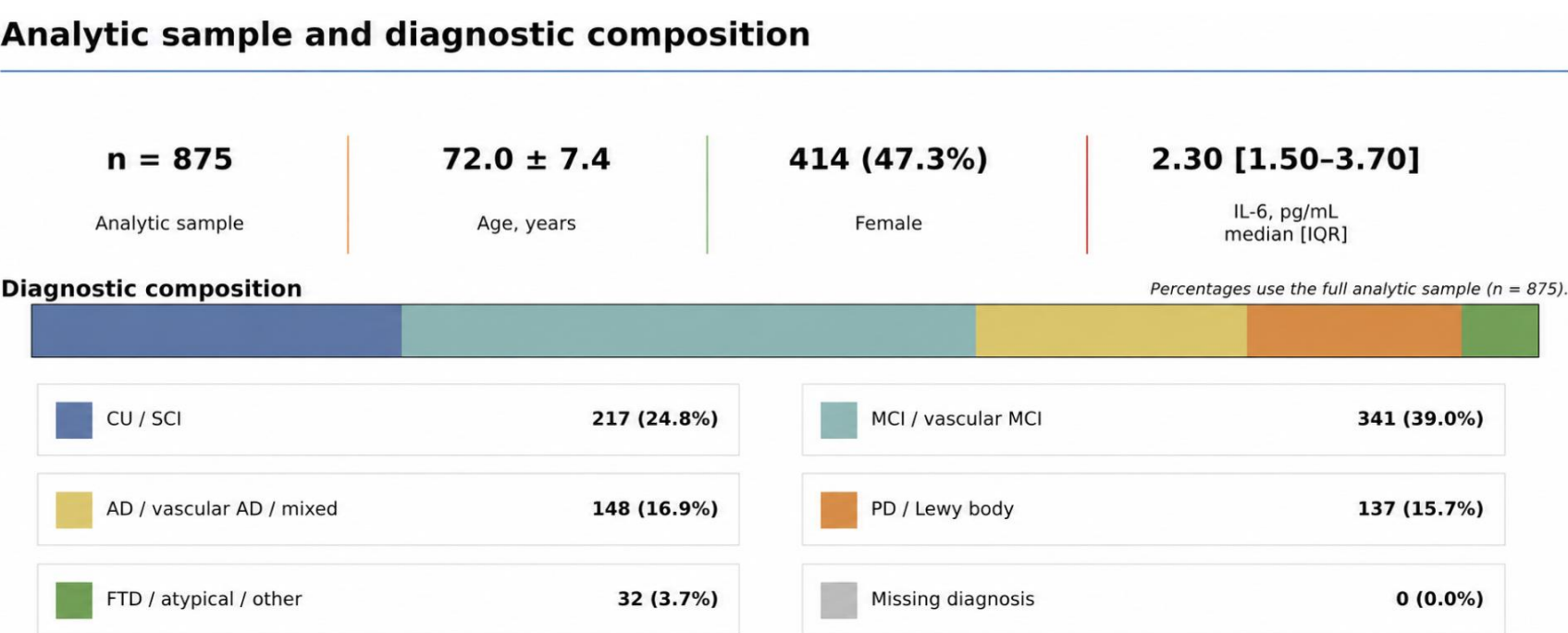


Figure 1. Analytic sample characteristics and diagnostic composition.

Diagnoses were available for all 875 participants and were collapsed into five clinically interpretable groups for display.

Supplement	Users / non-users	Mean IL-6, users	Mean IL-6, non-users	Adjusted β (95% CI)	Adjusted p
Omega-3	184 / 691	2.98	3.50	-0.055 (-0.123 to 0.013)	0.110
Probiotics	38 / 837	2.60	3.43	-0.113 (-0.215 to -0.011)	0.030
Glucosamine	58 / 817	2.74	3.44	-0.098 (-0.209 to 0.013)	0.083

Table 1. Age- and sex-adjusted associations between current supplement use and IL-6

β estimates compare current users with non-users on the log1p-transformed IL-6 scale. Negative β values indicate lower transformed IL-6 among users. Separate models were fitted for each supplement using HC3 robust standard errors.

Analyses were exploratory and p values were not adjusted for multiple comparisons; findings require confirmation in independent studies.

CONCLUSIONS

- All three supplement groups showed lower unadjusted IL-6, but the associations weakened after accounting for age and sex.
- Probiotic use showed the clearest age- and sex-adjusted association with lower IL-6 in this exploratory analysis.
- Omega-3 and glucosamine retained negative adjusted estimates, but the evidence was insufficient to distinguish these associations from chance.
- The small and highly imbalanced user groups, particularly probiotics and glucosamine, limit precision and make the findings vulnerable to influential observations.
- These cross-sectional results are hypothesis-generating and require confirmation using longitudinal data, validated supplement exposure measures, and broader control of health and lifestyle factors.

REFERENCES

- Lazou-Ahrén I, Björklund M, Molin G, et al. *Probiotic-Reduced Inflammaging in Older Adults: A Randomized, Double-Blind, Placebo-Controlled Trial. Probiotics and Antimicrobial Proteins*. Published online 2024. doi:10.1007/s12602-024-10310-7.
- Zhao L, Tang Z, Zhu C. *Serum interleukin-6 as a neuroinflammatory biomarker across the spectrum of neurological disorders: a large-scale retrospective cohort study of 6,465 individuals. Frontiers in Immunology*. 2026;17:1825206. doi:10.3389/fimmu.2026.1825206.
- Bohn L, Drouin SM, McFall GP, et al. *Machine learning analyses identify multi-modal frailty factors that selectively discriminate four cohorts in the Alzheimer’s disease spectrum: a COMPASS-ND study. BMC Geriatrics*. 2023;23:837. doi:10.1186/s12877-023-04546-1

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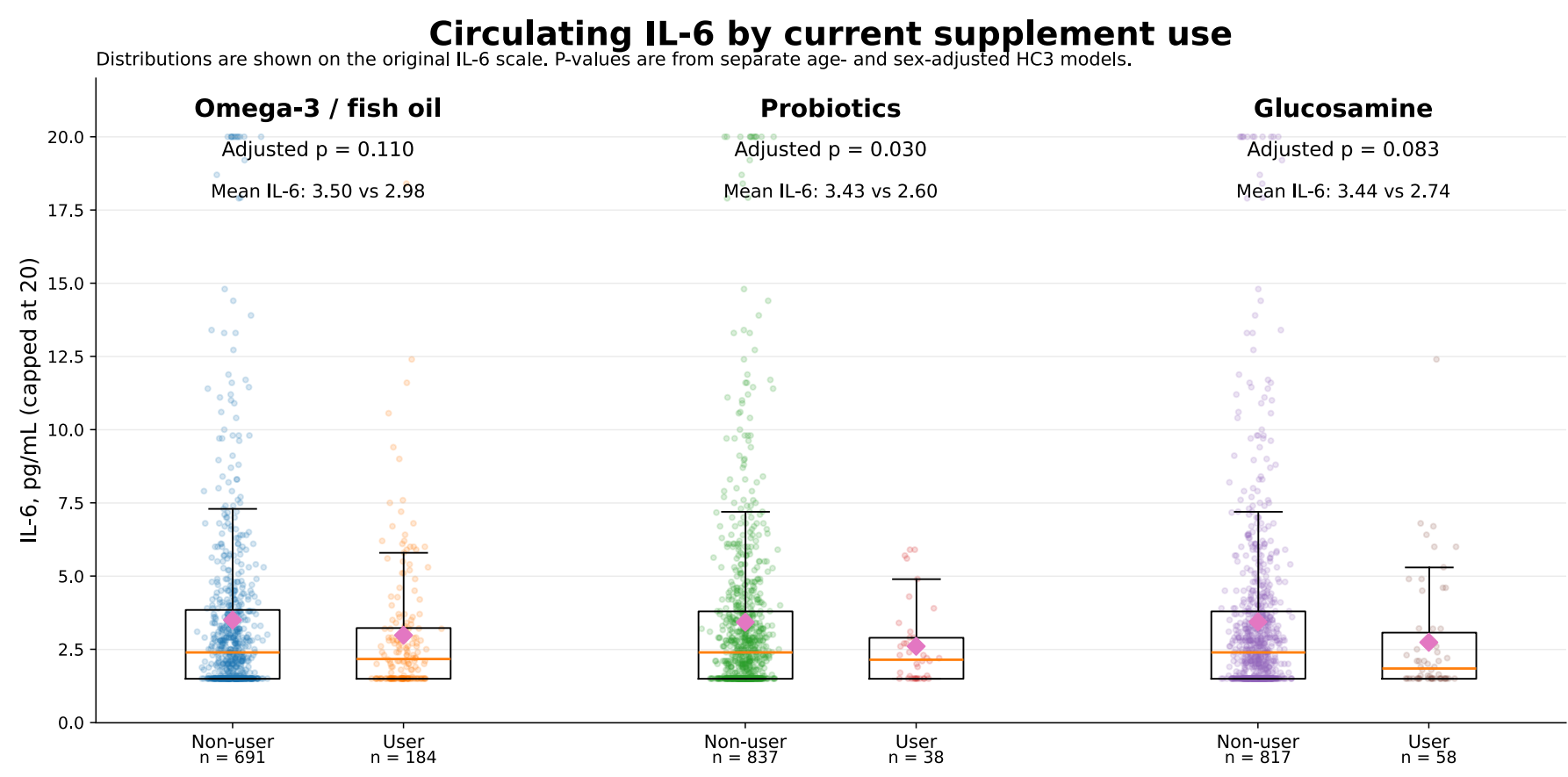


Figure 2. Distribution of circulating IL-6 among supplement users and non-users

Boxes show the median and interquartile range; diamonds indicate the mean; points represent individual participants. IL-6 was capped at 20 pg/mL for analysis and display. P values are from separate age- and sex-adjusted linear models of log1p-transformed IL-6 using HC3 robust standard errors.

Supplement categories were not mutually exclusive.

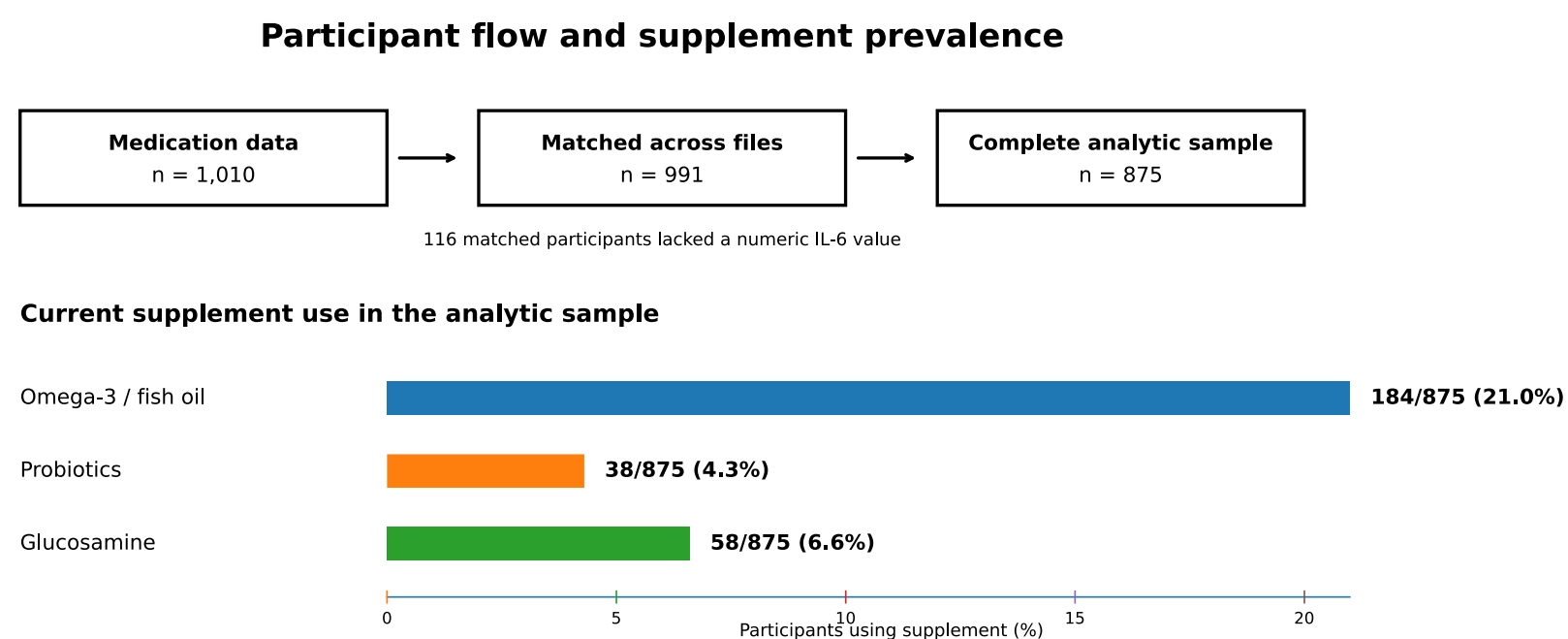


Figure 3. Participant flow and prevalence of current supplement use

Of 1,010 participants with current medication data, 991 were matched across the medication, demographic, and IL-6 files. The primary complete-case analysis included 875 participants with available age, sex, and numeric IL-6 data.