Validation and Comparison of Frailty Indexes: An OHDSI Network Study

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Background

A frailty index (FI) is a marker of overall health status and vulnerability, often used to identify those at increased risk for adverse health outcomes, such as hospitalization, disability, or death. It is typically calculated as a sum (or proportion) of health indicators – or deficits – across diverse health domains including chronic conditions, physical function, cognition, mental health, nutrition, and social participation. FIs vary in the number and type of included deficits, depending on the data source and intended application, with a minimum recommendation of 30 deficits[1].

In this exploratory project, we sought to validate and compare three electronic health record (EHR) FIs and one questionnaire-based FI across multiple healthcare settings and geographies, to understand the degree of frailty variability by FI metrics and geographic cohort. FIs were computed from individuals' diagnoses, prescriptions, procedures, and devices. We calculated FIs (and the contributing deficits) from five data sources, two from the UA and three from the UK.

Study design. A multinational multi-cohort study using routinely collected healthcare data, standardized to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) from five resources:

- IQVIA PharMetrics®, which includes commercial claims for inpatient and outpatient healthcare, and prescriptions from private health insurance for ~110 million people in the United States.
- All of Us (AoU) includes self-report surveys on personal demographics, health, and lifestyle, EHR from contributing regional health centers, federally qualified health centers, and Veterans Affairs medical centers, physical measurements (e.g., height, weight, blood pressure), and genomic data from biospecimens for a convenience sample of more than 400,000 participants from the United States.
- IQVIA Medical Research Data, primary care EHRs from the United Kingdom (IMRD-UK, version: 2022-09, 14M individuals), incorporating data from THIN, A Cegedim Database (reference made to THIN is intended to be descriptive of the data asset licensed by IQVIA)
- IMRD-EMIS, primary care EHRs from the United Kingdom (version: 2022-12, 5M individuals).
- The UK Biobank (UKBB)[2] is an ongoing prospective cohort study of over 500,000 participants, residents of England, Scotland, and Wales, recruited in 2006-2010 at the age of 40-69 years. Participants completed a set of questionnaires (e.g., diet and well-being), underwent a brief interview, and had their physical measurements and biological samples taken. Additionally, the EHRs of most participants have been processed and integrated.

The study population included all individuals whose EHR was available for ≥1 year of observation prior to an index date -- defined as a random visit for UK data sources and PharMetrics; and 1 year following recruitment date in the AoU data – where the person was at least 40 years old.

Frailty indexes. We considered two EHR derived FIs: the UK Electronic frailty index (eFI)[3] and the US Veterans Affairs Frailty Index (VA-FI)[4,5]. We computed all FIs based on a lookback period of 1 year[6] and, as a sensitivity analysis for the UK resources only, on a period of 10 years.

Statistical analysis. To assess the validity of the FIs in each data source, we computed the density and dispersion, frequency of deficits, and investigated trends in age and sex strata.[1] We also compared categorical frailty (robust, pre-frail, frail), based on published FI cut points across data sources.

Results

Table 1 shows summary statistics for each data source population. As an example, Figure 1 shows the prevalence of VA-FI pre-frail (score $\geq$ 0.11) and frail ($\geq$ 0.21) status, as well as example deficits osteoporosis and peripheral vascular disease (PVD). The direction of age and sex trends was consistent with the literature and across data sources, e.g., frailty (and pre-frailty) prevalence increased with age and was greater, for most age groups, in females than males. There were prevalence discrepancies across data sources that were unexpected and require deeper examination. Figure 2 demonstrates persistent prevalence discrepancies between 1-year lookback in US data, compared to 10-year lookback in UK data.

Table 1. Characteristics of study populations in the various data sources

	PharMetrics	AoU	IMRD-EMIS	IMRD-UK	UKBB
N	5,292,854	189,746	1,103,278	3,051,179	470,226
Female	2,838,483 (53.6%)	115,432 (60.6%)	551,869 (50.0%)	1,547,703 (50.7%)	252,859 (53.8%)
Age group					
40-45y	627,659 (11.9%)	17,775 (9.4%)	158,160 (14.3%)	430,175 (14.1%)	37,161 (7.9%)
45-50y	640,687 (12.1%)	19,170 (10.0%)	143,130 (13.0%)	407,660 (13.4%)	55,532 (11.8%)
50-55y	689,205 (13.0%)	23,609 (12.4%)	138,026 (12.5%)	388,155 (12.7%)	71,806 (15.3%)
55-60y	734,542 (13.9%)	28,287 (14.9%)	123,666 (11.2%)	355,399 (11.6%)	84,713 (18.0%)
60-65y	729,125 (13.8%)	28,288 (14.9%)	106,518 (9.7%)	319,114 (10.5%)	95,090 (20.2%)
65-70y	599,904 (11.3%)	26,956 (14.2%)	83,440 (7.6%)	256,147 (8.4%)	80,434 (17.1%)
70-75y	446,854 (8.4%)	22,301 (11.7%)	54,939 (5.0%)	158,664 (5.2%)	36,167 (7.7%)
75-80y	338,240 (6.4%)	13,565 (7.1%)	29,173 (2.6%)	66,204 (2.2%)	8,429 (1.8%)
>80	486,638 (9.2%)	9,795 (5.1%)	266,226 (24.1%)	669,661 (21.9%)	894 (0.2%)

Conclusion

In this study, we found substantial differences in frailty among included cohorts. These variations may arise from disparities in the overall health status of individuals between cohorts, but are more likely attributable to differences in the coding and reporting of health conditions within the various healthcare systems over time. As a result, while the OMOP CDM and OHDSI open-source software (e.g., FeatureExtraction) increasingly facilitate implementation of studies – involving comorbidity and frailty indices – across multinational network partners, more work is needed to evaluate and validate these established indices across the highly varied international health systems in order for these measures to be useful for identifying individuals with increased risk for adverse health outcomes.

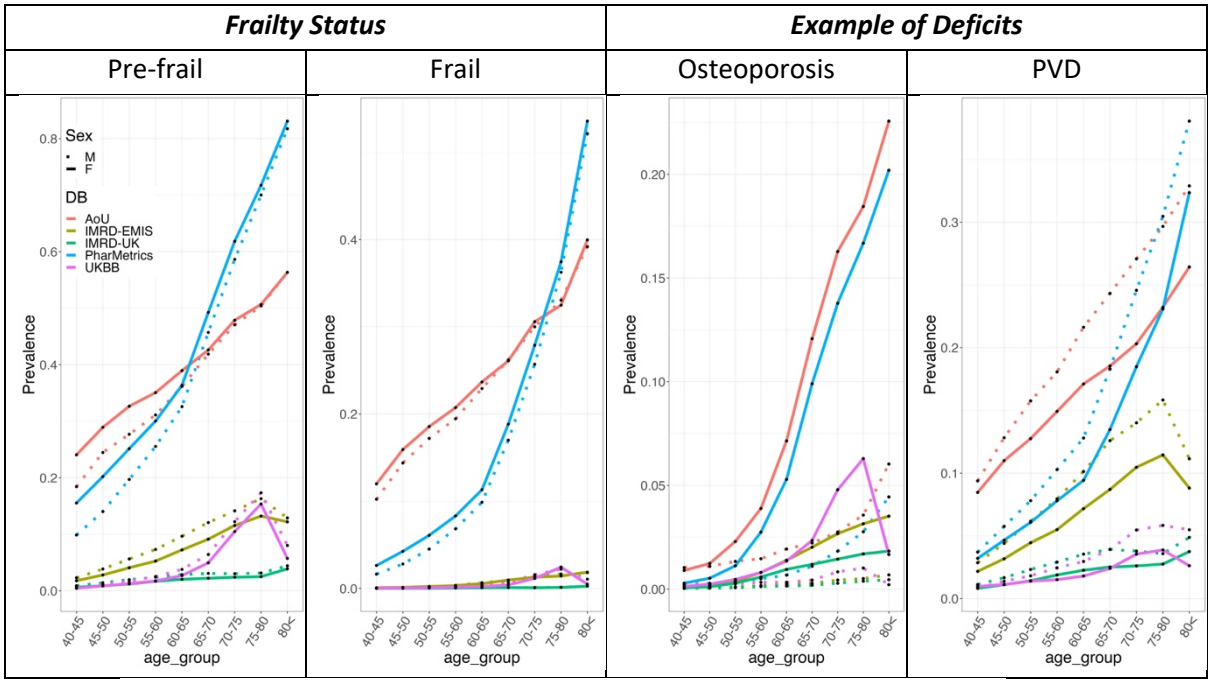

Figure 1. Comparison of sex-stratified prevalence of pre-frail and frail status, and examples of two deficits as a function of age across data sources. FIs computed in a lookback period of 1 year.

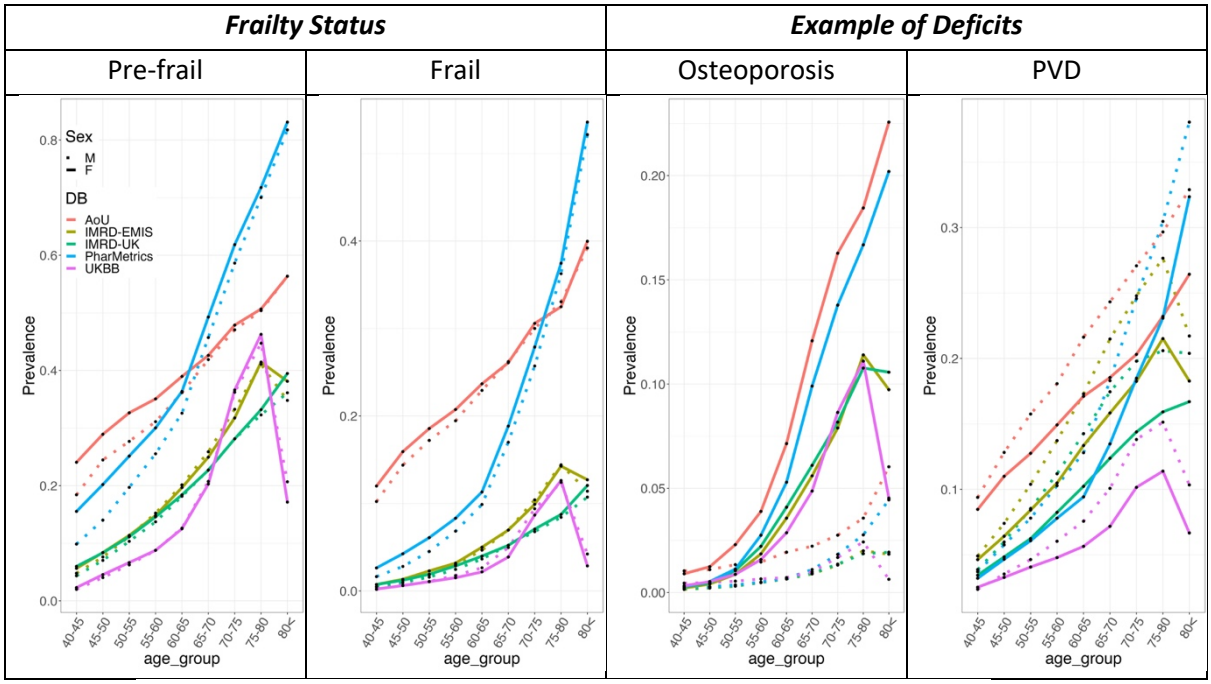

Figure 2. Comparison of sex-stratified prevalence of pre-frail and frail status, and examples of two deficits as a function of age across data sources. FIs computed in a lookback period of 1 year in the US resources and 10 years in the UK resources.

References

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