**Research Paper** 

# Frailty transitions in electronic health records: who first? what first?

# Fabienne Hershkowitz Sikron<sup>1</sup>, Rony Schenker<sup>2</sup>, Orit Shahar<sup>3</sup>, Achinoam Ben Akiva-Maliniak<sup>4</sup>, Galit Segal<sup>5</sup>, Yishay Koom<sup>6</sup>, Idit Wolf<sup>7</sup>, Bawkat Mazengya<sup>8</sup>, Maor Lewis<sup>9</sup>, Tzippy Shochat<sup>10</sup>, Dov Albukrek<sup>11</sup>

<sup>1</sup>Department of Epidemiology and Medical Quality Assessment, Meuhedet HMO, Tel-Aviv Yaffo 6203854, Israel <sup>2</sup>Director of Knowledge Development and Research, Joint-Eshel, 9 Eliezer Kaplan, Jerusalem 9103401, Israel <sup>3</sup>Director, Rehabilitation and Preservation of Functionality, Joint-Eshel, 9 Eliezer Kaplan, Jerusalem 9103401, Israel <sup>4</sup>Coordinator of Preservation of Functionality, Joint-Eshel, 9 Eliezer Kaplan, Jerusalem 9103401, Israel <sup>5</sup>Chief Geriatric Physician Meuhedet HMO, Tel-Aviv Yaffo 6203854, Israel <sup>6</sup>Director, Senior Citizen Department, Meuhedet HMO, Tel-Aviv Yaffo 6203854, Israel <sup>7</sup>Chief Geriatric Nurse, Meuhedet HMO, Tel-Aviv Yaffo 6203854, Israel <sup>8</sup>Data Analytics, Meuhedet HMO, Tel-Aviv Yaffo 6203854, Israel <sup>9</sup>MD, Medical Division, Meuhedet HMO, Tel-Aviv Yaffo 6203854, Israel <sup>10</sup>Research Institute, Meuhedet HMO, Tel-Aviv Yaffo 6203854, Israel <sup>11</sup>Chief Medical Officer, Meuhedet HMO, Tel-Aviv Yaffo 6203854, Israel

Correspondence to: Fabienne Hershkowitz Sikron; email: fabian hershkowitz@meuhedet.co.il Keywords: frailty transition, electronic frailty index, older people, health maintenance organization, statistics and numerical data Accepted: April 14, 2025 Published: May 12, 2025

Received: October 14, 2024

Copyright: © 2025 Hershkowitz Sikron et al. This is an open access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

## ABSTRACT

Background: Frailty is associated with an increased risk of adverse health outcomes and may worsen over time. Objectives: This study aims to describe the dynamic trajectory of frailty, identify the characteristics of those who deteriorate first, and determine what deteriorates first.

Study Design and Setting: A primary care longitudinal population-based cohort with repeated measures at baseline and one year later.

Participants: The cohort included all 119,952 Meuhedet members aged 65 years and over as of January 2023.

Predictors: Demographic factors, health indicators, and the Meuhedet Electronic Frailty Index containing 36 deficits.

Outcomes: Worsening frailty is defined as a higher frailty level one year later in 2024 compared to 2023. A new frailty deficit is defined as a deficit appearing in 2024 that was not present in 2023.

Statistical Analysis: The comparison of worsening percentages by demographic and clinical characteristics was tested using the chi-square test at the univariable level and logistic regression at the multivariable level.

Results: Overall, 13.3% of participants worsened after one year of follow-up, with 2.3% dying. Higher risk groups for worsening included females, older individuals, those belonging to the Arab sector, and those with multimorbidity. New deficits mainly included modifiable risk factors related to general health and functionality, despite chronic diseases being more frequent at baseline.

Conclusions: Emphasizing intervention programs based on these health promotion issues may significantly impact disease control and slow frailty worsening.

### **INTRODUCTION**

Emerging evidence suggests significant variability in the health status of older individuals, with people of the same age differing greatly in their vulnerability to adverse outcomes [1]. This variability is often referred to as frailty [2]. Geriatricians define frailty as a biological syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiological systems, causing vulnerability to adverse outcomes [3]. Frailty is associated with an increased risk of adverse health consequences, including falls [4], hospitalization [5, 6], and death [2, 7–9].

Based on the cumulative deficit model of Rockwood and Mitnitski [10, 11], an Electronic Frailty Index (EFI) has been developed and validated, allowing the classification of patients according to their level of frailty [12]. Today, the EFI is routinely adopted within all UK primary care settings [13, 14]. Since the operative definitions of such an index are specific to each country [15, 16], versions of the EFI have been developed in various countries, including the US [8, 17], Canada [18], Australia [19], China [20], Japan [21], Sweden [22, 23], and other parts of the United Kingdom such as Wales [24] and Scotland [25].

Frailty is not static; it is a dynamic health state that changes over time, even within a relatively short 12 months follow-up period [26]. It usually worsens but may also improve [2]. Despite the importance of the dynamic nature of frailty and its association with increased disability in terms of ADL [27], increased use of health care services [28], and all-cause mortality [29], studies on predictors of frailty worsening over time are sparse in the general geriatric literature [30, 31]. A meta-analysis by Kojima et al. showed pooled rates of frailty transition patterns among communitydwelling older people from 16 cohorts [32]. They found an association between older age and frailty worsening [33–35], and that women were more likely to change frailty status, either improving or worsening, rather than staying the same. Greater frailty at baseline increased the likelihood of worsening at follow-ups [36]. Multimorbidity was associated with frailty worsening among non-frail participants [31, 33], as well as polypharmacy [37, 38] and lower self-rated health [36, 39]. Physical inactivity [40], mobility impairment [39], and slow gait speed [26, 41] were also associated with frailty worsening. Social predictors such as fewer social interactions, living alone [42, 43], low education [31, 35, 44, 40], difficulty meeting living expenses [39], and being part of a minority [45] were also identified as predictors of frailty worsening. Other predictors of frailty worsening included psychological predictors such as depressed mood [46], sensory variables such as visual and hearing impairment [39], decreased cognitive activities [47], and cognitive impairment [37, 39].

Recently, our team developed an EFI according to our needs as an HMO, called MEFI (Meuhedet Electronic Frailty Index). MEFI contains 36 deficits, based on Clegg's items [12] and Orkaby's items [8]. MEFI was validated and has been proven to predict hospitalization and mortality [6], and was used to measure frailty and frailty worsening in this study.

It was found that an index based on the cumulative deficit model, such as the MEFI, better captures the multidimensional and dynamic nature of frailty over time [40], is considered a more accurate predictor of mortality [7], and is more sensitive to modifications in underlying health than the phenotype model [48]. A look at the predictors of frailty worsening, such as multimorbidity, activity limitation, or sensory impairment, reveals that they are all represented by one or more specific deficits included in MEFI (see Table 1). Using MEFI deficits to define predictors of frailty worsening is advantageous since they are routinely collected anyway, and the definition of the deficits is quite agreed upon beyond the various EFI in use in the literature. Unfortunately, no studies on predictors of frailty worsening, in terms of EFI deficits, could be found.

The objectives of this study are (1) to describe the dynamic trajectory of frailty, (2) to identify the characteristics of those who deteriorate first, and (3) to identify which deficits deteriorate first in each frailty level. A better understanding of frailty worsening among community-dwelling older adults will help define early warning indicators of who will worsen first and determine preventive measures focused on what will worsen first.

#### RESULTS

#### **Participants**

The cohort included all 119,952 patients of the Meuhedet HMO aged 65 and over, 54.4% of whom were females (See Table 2). The largest age group was those aged 65–74, with a mean age of 73.8 (SD = 7.0), a median of 72, a range from 65 to 106, and an interquartile range of 68 to 78. More than half belonged to the middle social level, and 8.3% belonged to the Arabic sector. Regarding frailty levels, 37.4% were fit, 40.3% were mildly frail, 16.8% were moderately frail, and 5.5% were severely frail. Regarding other aspects of their medical condition, 16.7% were hospitalized at least once the year before follow-up, 7.4% had a CCI score higher than 5, and 70% were overweight or obese.

### Table 1. List of 36 deficits included in the MEFI.

Deficits	
Activity Limitation	
Anaemia and Haematinic Deficiency	
Anxiety	
Arthritis	
Atrial Fibrillation	
Cancer (any except basal cell skin cancer)	
Cerebrovascular Disease	
Chronic Kidney Disease	
Coronary Artery Disease	
Dementias	
Depression	
Diabetes	
Dizziness/Vertigo	
Fall/fall-related injuries (hip/skull fractures, subdural hematoma)	
Fatigue	
Gait Abnormality	
Gastro-intestinal Disease	
Hearing Impairment	
Heart Failure	
Housebound	
Hypertension	
Lung Disease	
Memory and Cognitive Problems	
Muscular Wasting	
Osteoporosis	
Parkinson's Disease	
Peripheral Neuropathy	
Peripheral Vascular Disease	
Polypharmacy	
Requires Care	
Sleep Disturbance	
Social Vulnerability	
Thyroid Disease	
Urinary Incontinence	
Vision Comorbidity	
Weight Loss in the past year	

# Table 2. Baseline characteristics, worsening rates and crude OR.

<i>N</i> = <b>119,952</b>	Distribution at BL	Pct. worsened	
All	100% <i>N</i> = 119,952	within each sub-group**	
Sex			
Male	45.6%	13.1%*	
Female	54.4%	13.5%	

65-74 years         60.8%         10.0%           75-84 years         29.8%         16.2%           85- years         29.3%         25.0%           SES groups	Age groups		
85 + years         9.3%         25.6%           SES groups	65–74 years	60.8%	10.0%
SES groups           Low         25.3%         14.5%           Intermediate         54.1%         13.3%           High         20.6%         11.6%           Sector             Jewish secular         77.4%         13.2%           Jewish orthodox         14.2%         12.5%           Arabic         8.3%         15.9%           MEFT 2023             Fit         37.4%         11.9%           Mild fraily         40.3%         13.3%           Moderate frailty         16.8%         18.0%           Severe frailty         2.5%         8.9%           Ves         16.7%         18.6%           CCI groups             0         31.4%         8.4%           1-2         35.1%         13.5%           3-5         26.1%         16.8%           6+         7.9%         12.2%           Normal weight         2.84%         12.2%           Obesity         30.7%         14.0%           Top 15 deficits          12.5%           Normal weight         2.5%         16.5%           Diabetes	75–84 years	29.8%	16.2%
Low         25.3%         14.5%           Intermediate         54.1%         13.3%           High         0.0%         11.6%           Sector	85+ years	9.3%	25.6%
Intermediate         54.1%         13.3%           High         20.6%         11.6%           Sector	SES groups		
High     20.6%     11.6%       Sector         Jewish scular     77.4%     13.2%       Jewish orthodox     14.2%     12.5%       Arabic     8.3%     15.9%       MEFI 2023         Fit     37.4%     11.9%       Mild frailty     40.3%     13.3%       Moderate frailty     16.8%     18.0%       Severe frailty     5.5%     8.9%       Hosp. year before         No     83.3%     12.3%       Yes     16.7%     18.6%       CCI groups         0     31.4%     8.4%       1-2     35.1%     13.5%       3-5     26.1%     16.8%       6+     7.4%     21.1%       BM groups         Underweight     1.6%     12.2%       Normal weight     28.4%     13.2%       Overweight     39.4%     12.6%       Obsity     39.4%     12.6%       Obsity     39.4%     12.6%       Obsity     39.4%     12.6%       Overweight     5.3%     15.2%       Hypertension     72.9%     15.0%       Arthritis     53.3%     15.2%	Low	25.3%	14.5%
Sector         Jewish secular         77.4%         13.2%           Jewish secular         77.4%         12.5%           Jewish orthodox         14.2%         12.5%           Arabic         8.3%         15.9%           MEFI 2023             Fit         37.4%         11.9%           Mild frailty         40.3%         13.3%           Moderate frailty         5.5%         8.9%           Severe frailty         5.5%         8.9%           Hosp. year before             No         83.3%         12.3%           Yes         16.7%         18.6%           CCI groups             0         31.4%         8.4%           1-2         35.1%         13.5%           3-5         26.1%         16.8%           6+         7.4%         21.1%           BMI groups          14.2%           Underweight         1.6%         21.2%           Overweight         30.7%         14.4%           Hypertension         72.9%         15.2%           Diabetes         32.7%         15.2%           Diabetes	Intermediate	54.1%	13.3%
Jewish secular         77.4%         13.2%           Jewish orthodox         14.2%         12.5%           Arabic         8.3%         15.9%           MEFT 2023         """"""""""""""""""""""""""""""""""""	High	20.6%	11.6%
Jewish orthodox         14.2%         12.5%           Arabic         8.3%         15.9%           MEFT 2023             Fit         37.4%         11.9%           Mild frailty         40.3%         13.3%           Moderate frailty         16.8%         18.0%           Severe frailty         5.5%         8.9%           Hosp, year before          12.3%           No         83.3%         12.3%           Yes         16.7%         18.6%           CCI groups             0         31.4%         8.4%           1-2         35.1%         13.5%           3-5         26.1%         16.8%           6+         7.4%         21.1%           BMI groups          12.2%           Underweight         1.6%         12.6%           Overweight         39.4%         12.2%           Obesity         30.7%         14.0%           Hypertension         72.9%         15.7%           Social vulnerability         27.5%         16.6%           Lung disease         24.8%         15.8%           Memory/cognitive         2	Sector		
Arabic       8.3%       15.9%         MEFI 2023           Fit       37.4%       11.9%         Mild frailty       40.3%       13.3%         Moderate frailty       16.8%       18.0%         Severe frailty       5.5%       8.9%         Hosp. year before           No       83.3%       12.3%         Yes       16.7%       18.6%         CCI groups           0       31.4%       8.4%         1-2       35.1%       13.5%         3-5       26.1%       16.6%         6+       7.4%       21.1%         BMI groups        1.6%       21.2%         Underweight       1.6%       21.2%       0%         Overweight       30.7%       14.0%       14.3%         Hypertension       72.9%       15.0%       15.0%         Diabetes       32.7%       15.7%       15.6%         Diabetes       32.7%       15.7%       16.6%         Lung disease       24.8%       15.8%       16.6%         Memory/cognitive       24.8%       15.8%       16.6%         Memory/cog	Jewish secular	77.4%	13.2%
MEF1 2023           Fit         37.4%         11.9%           Mild frailty         40.3%         13.3%           Moderate frailty         16.8%         18.0%           Severe frailty         5.5%         8.9%           Hosp, ear before          12.3%           No         83.3%         12.3%           Yes         16.7%         18.6%           CCI groups          84.6%           CCI groups          1.4%           0         31.4%         8.4%           1-2         35.1%         13.5%           3-5         26.1%         16.8%           6+         7.4%         21.1%           BM groups          12.2%           Underweight         1.6%         12.2%           Overweight         39.4%         13.2%           Obesity         30.7%         14.0%           Polypharmacy         89.2%         14.3%           Hypertension         72.9%         15.0%           Arthritis         55.3%         15.2%           Diabetes         32.7%         16.6%           Lung disease         24.8%         15.8%	Jewish orthodox	14.2%	12.5%
Fit     37.4%     11.9%       Mild frailty     40.3%     13.3%       Moderate frailty     16.8%     18.0%       Severe frailty     16.8%     18.0%       Severe frailty     16.8%     18.0%       Hosp. year before     1     1       No     83.3%     12.3%       Yes     16.7%     18.6%       CCI groups     1     1       0     31.4%     8.4%       1-2     35.1%     13.5%       3-5     26.1%     16.8%       6+     7.4%     21.1%       BMI groups     1     1.6%       Underweight     1.6%     21.2%       Normal weight     28.4%     13.2%       Overweight     39.4%     14.3%       Hypertension     72.9%     15.0%       Arthritis     55.3%     15.2%       Diabetes     32.7%     15.6%       Lung disease     24.8%     15.8%       Memory/cognitive     24.1%     19.6%       PVD     23.7%     17.6%       Goronary Artery     22.2%     16.8%       Gl disease     22.2%     16.8%       Gl disease     21.1%     14.9%       Grupoid disease     21.1%     14.9% <tr< td=""><td>Arabic</td><td>8.3%</td><td>15.9%</td></tr<>	Arabic	8.3%	15.9%
Mild fraily         40.3%         13.3%           Moderate fraily         16.8%         18.0%           Severe fraily         5.5%         8.9%           Hosp, year before             No         83.3%         12.3%           Yes         16.7%         18.6%           CCI groups             0         31.4%         8.4%           1-2         35.1%         13.5%           3-5         26.1%         16.8%           6+         7.4%         21.2%           Normal weight         1.6%         21.2%           Normal weight         28.4%         13.2%           Overweight         39.4%         12.6%           Obesity         39.4%         12.6%           Overweight         39.4%         12.6%           Overweight         39.4%         15.0%           Top 15 deficits         15.0%         15.0%           Polypharmacy         89.2%         15.3%           Hypertension         72.9%         15.0%           Arthritis         55.3%         15.2%           Diabetes         32.7%         16.6%           PVD         23	MEFI 2023		
Moderate frailty         16.8%         18.0%           Severe frailty         5.5%         8.9%           Hosp. year before	Fit	37.4%	11.9%
Severe fraily         5.5%         8.9%           Hosp. year before	Mild frailty	40.3%	13.3%
Hosp. year before         No         83.3%         12.3%           Yes         16.7%         18.6%           CCI groups         1         18.6%           0         31.4%         8.4%           1–2         35.1%         13.5%           3–5         26.1%         21.1%           6+         7.4%         21.1%           BMI groups         1         1.6%         21.2%           Underweight         1.6%         21.2%           Normal weight         28.4%         13.2%           Overweight         39.4%         12.6%           Overweight         39.4%         12.6%           Overweight         39.4%         13.2%           Overweight         39.4%         12.6%           Diabetes         32.7%         14.3%           Hypertension         72.9%         16.6%           Lung disease         24.8%         15.8%	Moderate frailty	16.8%	18.0%
No         83.3%         12.3%           Yes         16.7%         18.6%           CCI groups          18.6%           0         31.4%         8.4%           1-2         35.1%         13.5%           3-5         26.1%         16.8%           6+         7.4%         21.1%           BMI groups          1           Underweight         1.6%         21.2%           Normal weight         28.4%         13.2%           Overweight         30.7%         14.0%           Top 15 deficits         1         14.0%           Polypharmacy         89.2%         14.3%           Hypertension         72.9%         15.0%           Arthritis         55.3%         15.2%           Diabetes         32.7%         15.6%           Lung disease         24.8%         15.8%           Memory/cognitive         24.1%         19.6%           PVD         23.7%         16.6%           GI disease         22.2%         14.3%           Thyroid disease         21.1%         14.7%           Cancer         21.1%         14.7%           Carcer         21.1% <td>Severe frailty</td> <td>5.5%</td> <td>8.9%</td>	Severe frailty	5.5%	8.9%
Yes         16.7%         18.6%           CCI groups	Hosp. year before		
CCI groups       31.4%       8.4%         1-2       35.1%       13.5%         3-5       26.1%       16.8%         6+       7.4%       21.1%         BMI groups       1       1.6%       21.2%         Underweight       1.6%       21.2%       39.4%       13.2%         Overweight       39.4%       12.6%       30.7%       14.0%         Overweight       39.4%       12.6%       30.7%       14.0%         Top 15 deficits       1       1       1.6%       1.6%       1.6%         Polypharmacy       89.2%       14.3%       1.5.0%       <	No	83.3%	12.3%
0         31.4%         8.4%           1-2         35.1%         13.5%           3-5         26.1%         16.8%           6+         7.4%         21.1%           BMI groups         1         1.6%         21.2%           Underweight         1.6%         21.2%         32.4%         13.2%           Overweight         39.4%         12.6%         32.4%         32.4%         32.4%           Obesity         30.7%         14.0%         14.0%         14.3%         14.0%         14.3%         14.3%         14.3%         15.0%         14.3%         15.0%         16.6%         10.0%         10.0%         10.0%         10.0%         10.0%         10.0%         10.0%         10.0%         10.0%	Yes	16.7%	18.6%
1-2       35.1%       13.5%         3-5       26.1%       16.8%         6+       7.4%       21.1%         BMI groups           Underweight       1.6%       21.2%         Normal weight       28.4%       13.2%         Overweight       39.4%       12.6%         Obesity       30.7%       14.0%         Top 15 deficits           Polypharmacy       89.2%       14.3%         Hypertension       72.9%       15.0%         Arthritis       55.3%       15.2%         Diabetes       32.7%       15.6%         Kemory/cognitive       24.1%       19.6%         PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	CCI groups		
3-5       26.1%       16.8%         6+       7.4%       21.1% <b>BMI groups</b> 1.6%       21.2%         Underweight       1.6%       21.2%         Normal weight       28.4%       13.2%         Overweight       39.4%       12.6%         Obesity       30.7%       14.0% <b>Top 15 deficits</b> 1       1         Polypharmacy       89.2%       14.3%         Hypertension       72.9%       15.0%         Arthritis       55.3%       15.2%         Diabetes       32.7%       16.6%         Lung disease       24.8%       15.8%         Memory/cognitive       24.1%       19.6%         PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	0	31.4%	8.4%
6+         7.4%         21.1%           BMI groups         1.6%         21.2%           Underweight         1.6%         21.2%           Normal weight         28.4%         13.2%           Overweight         39.4%         12.6%           Obesity         30.7%         12.6%           Obesity         30.7%         14.3%           For J5 deficits         92.9%         14.3%           Hypertension         72.9%         15.0%           Arthritis         55.3%         15.2%           Diabetes         32.7%         15.6%           Lung disease         24.8%         15.8%           PVD         23.7%         16.6%           PVD         23.7%         17.0%           Coronary Artery         22.2%         16.8%           GI disease         22.2%         14.9%           Thyroid disease         21.1%         14.7%           Cancer         21.1%         16.9%           Cerebrovascular TI         18.3%         17.5%	1–2	35.1%	13.5%
BMI groups         1.6%         21.2%           Normal weight         28.4%         13.2%           Overweight         39.4%         12.6%           Obesity         39.4%         14.3%           Polypharmacy         89.2%         14.3%           Hypertension         72.9%         15.0%           Arthritis         55.3%         15.2%           Diabetes         32.7%         15.6%           Lung disease         24.8%         15.8%           Memory/cognitive         24.1%         19.6%           PVD         23.7%         17.0%           Coronary Artery         22.2%         16.8%           GI disease         21.1%         14.7%           Cancer         21.1%         16.9%           Cerebrovascular TI         18.3%         17.5%	3–5	26.1%	16.8%
Underweight         1.6%         21.2%           Normal weight         28.4%         13.2%           Overweight         39.4%         12.6%           Obesity         30.7%         14.0%           Top 15 deficits         7         7           Polypharmacy         89.2%         14.3%           Hypertension         72.9%         15.0%           Arthritis         55.3%         15.2%           Diabetes         32.7%         15.7%           Social vulnerability         27.5%         16.6%           Lung disease         24.8%         15.8%           Memory/cognitive         24.1%         19.6%           PVD         23.7%         17.0%           Coronary Artery         22.2%         16.8%           GI disease         22.2%         14.9%           Thyroid disease         21.1%         14.7%           Cancer         21.1%         16.9%           Cerebrovascular TI         18.3%         17.5%	6+	7.4%	21.1%
Normal weight         28.4%         13.2%           Overweight         39.4%         12.6%           Obesity         30.7%         14.0%           Top 15 deficits         7         7           Polypharmacy         89.2%         14.3%           Hypertension         72.9%         15.0%           Arthritis         55.3%         15.2%           Diabetes         32.7%         15.7%           Social vulnerability         27.5%         16.6%           Lung disease         24.8%         15.8%           Memory/cognitive         24.1%         19.6%           PVD         23.7%         17.0%           Coronary Artery         22.2%         16.8%           GI disease         21.1%         14.7%           Cancer         21.1%         16.9%           Cerebrovascular TI         18.3%         17.5%	BMI groups		
Overweight Obesity         39.4%         12.6%           Obesity         30.7%         14.0%           Top 15 deficits	Underweight	1.6%	21.2%
Obesity         30.7%         14.0%           Top 15 deficits         14.3%           Polypharmacy         89.2%         14.3%           Hypertension         72.9%         15.0%           Arthritis         55.3%         15.2%           Diabetes         32.7%         15.7%           Social vulnerability         27.5%         16.6%           Lung disease         24.8%         15.8%           PVD         23.7%         17.0%           Coronary Artery         22.2%         16.8%           GI disease         21.1%         14.7%           Cancer         21.1%         16.9%           Cerebrovascular TI         18.3%         17.5%	Normal weight	28.4%	13.2%
Fop 15 deficits         Polypharmacy       89.2%       14.3%         Hypertension       72.9%       15.0%         Arthritis       55.3%       15.2%         Diabetes       32.7%       15.7%         Social vulnerability       27.5%       16.6%         Lung disease       24.8%       15.8%         Memory/cognitive       24.1%       19.6%         PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Overweight	39.4%	12.6%
Polypharmacy       89.2%       14.3%         Hypertension       72.9%       15.0%         Arthritis       55.3%       15.2%         Diabetes       32.7%       15.7%         Social vulnerability       27.5%       16.6%         Lung disease       24.8%       15.8%         Memory/cognitive       24.1%       19.6%         PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Obesity	30.7%	14.0%
Hypertension72.9%15.0%Arthritis55.3%15.2%Diabetes32.7%15.7%Social vulnerability27.5%16.6%Lung disease24.8%15.8%Memory/cognitive24.1%19.6%PVD23.7%17.0%Coronary Artery22.2%16.8%GI disease22.2%14.9%Thyroid disease21.1%14.7%Cancer21.1%16.9%Cerebrovascular TI18.3%17.5%	Top 15 deficits		
Arthritis55.3%15.2%Diabetes32.7%15.7%Social vulnerability27.5%16.6%Lung disease24.8%15.8%Memory/cognitive24.1%19.6%PVD23.7%17.0%Coronary Artery22.2%16.8%GI disease22.2%14.9%Thyroid disease21.1%14.7%Cancer21.1%16.9%Cerebrovascular TI18.3%17.5%	Polypharmacy	89.2%	14.3%
Diabetes       32.7%       15.7%         Social vulnerability       27.5%       16.6%         Lung disease       24.8%       15.8%         Memory/cognitive       24.1%       19.6%         PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Hypertension	72.9%	15.0%
Social vulnerability       27.5%       16.6%         Lung disease       24.8%       15.8%         Memory/cognitive       24.1%       19.6%         PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       22.2%       14.9%         Thyroid disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Arthritis	55.3%	15.2%
Lung disease       24.8%       15.8%         Memory/cognitive       24.1%       19.6%         PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       22.2%       14.9%         Thyroid disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Diabetes	32.7%	15.7%
Memory/cognitive       24.1%       19.6%         PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       22.2%       14.9%         Thyroid disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Social vulnerability	27.5%	16.6%
PVD       23.7%       17.0%         Coronary Artery       22.2%       16.8%         GI disease       22.2%       14.9%         Thyroid disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Lung disease	24.8%	15.8%
Coronary Artery       22.2%       16.8%         GI disease       22.2%       14.9%         Thyroid disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Memory/cognitive	24.1%	19.6%
GI disease22.2%14.9%Thyroid disease21.1%14.7%Cancer21.1%16.9%Cerebrovascular TI18.3%17.5%	PVD	23.7%	17.0%
Thyroid disease       21.1%       14.7%         Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	Coronary Artery	22.2%	16.8%
Cancer       21.1%       16.9%         Cerebrovascular TI       18.3%       17.5%	GI disease	22.2%	14.9%
Cerebrovascular TI 18.3% 17.5%	-	21.1%	14.7%
		21.1%	16.9%
Kidney 14.1% 19.1%			
-	Kidney	14.1%	19.1%
Atrial Fibrillation 12.1% 19.7%	Atrial Fibrillation	12.1%	19.7%

\*Pearson Chi-Square, p < 0.05. \*\*Pearson Chi-Square, p < 0.001.

#### Worsening and frailty transitions

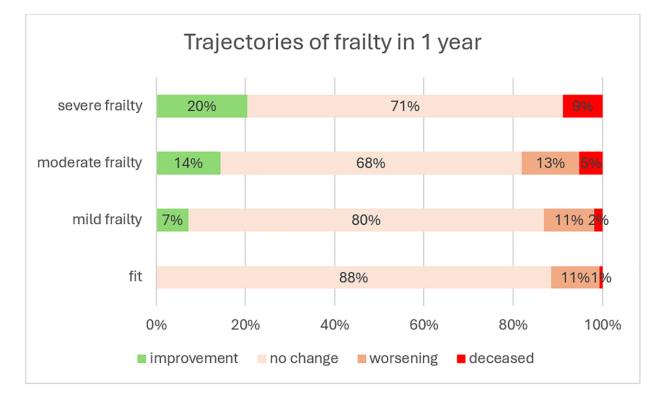
Overall, 13.3% of the cohort experienced worsening of their MEFI after one year of follow-up, and 2.3% had died. The worsening rate, including those who were deceased, was 11.9%, 13.3%, 18.0%, and 8.9% among the fit, mildly frail, moderately frail, and severely frail, respectively. The deceased rate was 0.6%, 1.9%, 5.2%, and 8.9%, respectively (see Figure 1). Estimated transitions from fit to any level of frailty were 10.2% for those aged 65–74, 17.2% for those aged 75–84, and 32.2% for those aged 85+. The worse the frailty was at baseline, the higher the percentage of dying. In each frailty level at baseline, people were likely to remain in their current frailty category, and transitions between adjacent frailty levels were more frequent than those across several frailty levels.

#### Predictors of worsening - WHO will worsen first

The worsening rate, including those who died, was 13.5% for females and 13.1% for males (p < 0.001). It increased with age, from 10.0% to 16.2% and 25.6% among the age groups 65–74, 75–84, and 85+, respectively (p < 0.001). The worsening rate decreased as socio-economic status increased, from 14.5% to 11.6%, and was higher among the Arabic sector (15.9%) compared to the general secular Jewish sector (13.2%) (p < 0.001). The worsening rate increased with frailty level at baseline, from 11.9% among the fit to

13.3% among the mildly frail, 18.0% among the moderately frail, and then declined to 8.8% among the severely frail (p < 0.001). The death rate increased with frailty level, at 0.6%, 1.9%, 5.2%, and 8.8% among the fit, mild, moderate, and severe frailty groups, respectively (worsening among the severe frailty group means they died). Those who had a previous hospitalization during the year 2022 had a worsening rate of 18.6%, a 52% higher rate than those who were not hospitalized (p < 0.001). Higher CCI scores showed a higher worsening rate, from 8.4% to 13.5%, 16.8%, and 21.1% for the fit, mild frailty, moderate frailty, and severe frailty, respectively (p < 0.001). The baseline deficits in January 2023 most associated with worsening, with a crude OR >1.5 or lower than 0.5, were, in decreasing order: polypharmacy, dementia, housebound, heart failure, memory and cognitive problems, hypertension, atrial fibrillation, kidney diseases. fall-related, activity limitation, sleep disturbance, and requirement for care.

A multivariate analysis conducted to determine factors associated with frailty worsening revealed that being female (OR = 1.18; 95% CI: 1.13, 1.22), being older (aged 75–84 vs. age 65–74: OR = 1.72; 95% CI: 1.65, 1.80); aged 85+ vs. age 65–74: OR = 2.80; 95% CI: 2.63, 2.98), and belonging to the Arabic sector (OR = 1.11; 95% CI: 1.04, 1.19), were associated with increased odds of frailty worsening at 1 year (see Table 3). Conversely, socio-economic status was associated



#### Figure 1. Trajectories of frailty in 1 year.

	Crude OR	aOR*	95% CI-OR**	Sig
Sex				
Male	Reference	Reference		
Female	1.03	1.18	1.13-1.20	<.001
Age groups				
65–74 years	Reference	Reference		
75–84 years	1.62	1.72	1.65-1.79	<.001
85+ years	2.56	2.80	2.63-2.98	<.001
SES groups				
Low	Reference	Reference		
Intermediate	0.91	0.91	0.87-0.95	<.001
High	0.80	0.77	0.72-0.82	<.001
Sector				
Jewish secular	Reference	Reference		
Jewish orthodox	0.95	0.91	0.86-0.96	<.001
Arabic	1.21	1.11	1.04-1.19	<.001
MEFI 2023				
Fit	Reference	Reference		
Mild frailty	1.12	0.57	0.54-0.60	<.001
Moderate frailty	1.51	0.45	0.42-0.48	<.001
Severe frailty	0.74	0.12	0.10-0.13	<.001
Hosp. year before				
No	Reference	Reference		
Yes	1.52	1.41	1.35-1.48	<.001
CCI groups				
0	Reference	Reference		
1–2	1.62	1.74	1.66-1.83	<.001
3–5	2.01	2.57	2.42-2.73	<.001
6+	2.52	4.01	3.68-4.37	<.001
BMI groups				
Underweight	1.61	0.56	0.50-0.64	<.001
Normal weight	Reference	Reference		
Overweight	0.96	0.53	0.47–0.60	0.42
Obesity	1.06	0.58	0.51-0.66	<.001
Comorbidity				
Act. Limitation	0.34	0.33	0.25-0.43	<.001
Atrial Fibrillation	1.58	1.59	1.51-1.68	<.001
Dementia	2.03	1.734	1.63-1.86	<.001
Fall Related	0.63	0.61	0.54-0.69	<.001
Heart Failure	1.74	1.60	1.51-1.70	<.001
Housebound	2.00	1.83	1.71-1.97	<.001
Hypertension	1.68	1.66	1.58-1.74	<.001
Kidney disease	1.54	1.39	1.32-1.47	<.001
Memory/Cognitive	1.73	2.23	2.13-2.33	<.001
Polypharmacy	2.75	2.87	2.63-3.13	<.001
Require for Care	0.10	0.05	0.02-0.13	<.001
Sleep disturbance	0.29	0.33	0.27-0.41	<.001

# Table 3. Multivariate logistic regression models for frailty worsening 1 year later.

\*aOR, odds ratio adjusted for other listed variables. \*\*All the aOR were significant at p < 0.001.

with decreased odds of frailty worsening (SES intermediate vs. low: OR = 0.91; 95% CI: 0.87, 0.95); (SES high vs. low: OR = 0.77; 95% CI: 0.72, 0.82). Higher frailty was associated with lower odds of worsening, compared with the fit level (mild: OR = 0.33; 95% CI: 0.32, 0.35); (moderate 65–74: OR = 0.15; 95% CI: 0.14, 0.16); (severe: OR = 0.02; 95% CI: 0.02, 0.02). The underweight group (OR = 0.56; 95% CI: 0.50, 0.64), the overweight group (OR = 0.53; 95%CI: 0.47, 0.60), and the obese group (OR = 0.58; 95% CI: 0.51, 0.66) had higher odds of worsening, compared with normal weight. Hospitalization during the year before, and higher CCI score, were also predictors for a worsened frailty transition after 1 year (OR = 1.41; 95%) CI: 1.35, 1.48). The deficits in 2023 with a crude OR higher than 1.5 or lower than 0.5 at the univariable level were also included in the model. Risk groups with the highest odds of worsening, in descending order, were those with polypharmacy, memory and cognitive problems, housebound, dementia, hypertension, heart failure, and atrial fibrillation. The c-index for discrimination was 0.734, as measured by Harrell's concordance index (CI95%: 0.729-0.738). There was no multicollinearity between the predictors, with variance in inflation factors (VIFs) less than 3.

#### New deficits - WHAT will worsen first

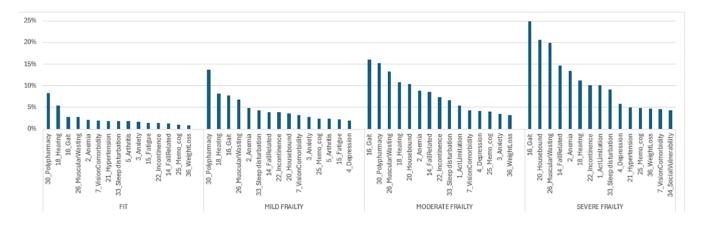
Among the 117,141 patients alive at the end of the follow-up, 38.0% were fit, 40.5% had mild frailty, 16.3% had moderate frailty, and 5.1% had severe frailty at the beginning of the follow-up.

At baseline, chronic diseases had the highest prevalence in all frailty groups. Among the fit, mild frailty, moderate frailty, and severe frailty groups, hypertension was reported in 48.9%, 83.2%, 93.7%, and 97.7%, respectively, followed by arthritis in 31.8%, 63.7%, 78.5%, and 88.0%, respectively. Other chronic diseases such as diabetes, lung disease, peripheral vascular

disease, and coronary artery disease were also prevalent in each frailty group. However, when looking at the prevalence of new deficits that emerged during the follow-up year, in descending order, most chronic diseases appeared in the lower half of the list. Figure 2 summarizes the top 15 new deficits stratified by frailty. Eight of the deficits appeared in all four frailty groups: gait abnormality, hearing impairment, muscular wasting, anemia, sleep disturbance, incontinence, vision comorbidity, and memory and cognitive problems. The percentage of new deficits increased with frailty level; for example, gait abnormality appeared as a new deficit in 3% of the fit, 8% of the mild, 16% of the moderate, and 25% of the severe frailty groups. Hearing impairment appeared as a new deficit in 6% of the fit, 8% of the mild, and 11% of the moderate and severe frailty groups. When stratifying by age at baseline within each frailty level, most of the top 15 deficiencies beyond age also appeared in each age group. The number of deficits in common with the top 15 list was 14, 14, and 12 among the mild group, 14, 13, and 11 among the mild frailty group, 14, 15, and 14 among the moderate frailty group, and 13, 14, and 15 among the severe frailty group, within those aged 65-74, 75-84, and 85+, respectively (see Supplementary Table 1).

#### DISCUSSION

Our paper aims to better understand the dynamics of worsening frailty, focusing on the scope of the issue, identifying who deteriorates first, and determining which deficits are likely to deteriorate first. The ultimate goal is to enhance the quality of care we provide for our patients. By understanding the frequency of frailty deterioration, we can grasp the urgency of taking action. Knowing who deteriorates first allows us to focus our efforts, and identifying what deteriorates first helps us prioritize issues for intervention. Preventing frailty deterioration can be beneficial at the individual clinical care level, in population management





by identifying risk groups, and in developing intervention programs that address the most likely problems.

Our first objective was to describe the dynamic trajectory of frailty over one year of follow-up. We found that 12% of fit individuals worsened, and among those with mild frailty, 7% improved, 80% remained in the same frailty category, and 13% worsened. This outcome is very similar to the worsening rate observed in Thompson's cohort, which was computed to an annual transition rate by Kaskirbayeva [31, 33]. Estimated transitions from fit to any level of frailty were higher in the Walsh cohort, likely due to the younger age of the cohort in our study, but the rates were proportionally almost identical to our cohort [45]. The similarity with these cohorts, which also used community-dwelling participants and an EFI to measure frailty, strengthens and validates our worsening measure. Our second objective was to identify who deteriorates first. We found that 13.3% worsened after one year of follow-up, with higher worsening prevalence among females, older individuals, those with lower socioeconomic levels, and those with comorbidities. Our findings align with the literature, including the debate about the association between sex and deterioration. Kojima's systematic review and meta-analysis found that women change more in both directions [7]. This is consistent with our findings: a higher rate of worsening among females than males (13.5% vs. 13.1%, respectively) and a higher rate of improvement among females than males (7.0% vs. 5.8%, respectively). We also observed that the worsening rate increased with the frailty level, consistent with the literature, but we noted a decline among the severe frailty group. This aligns with the finding that the longest period spent within the same frailty category is among the severely frail [45]. Although a negative relationship between baseline frailty and frailty worsening was found in the multivariate analysis, the positive relationship observed in the univariate analysis reappeared when the model was not controlled for age and comorbidity. Our third objective was to identify what deteriorates first at each frailty level. Among patients alive at the end of follow-up, although chronic diseases had the highest prevalence at baseline, there were few new cases of chronic diseases. This can be explained by the evidence that chronic diseases mostly occur before age 65 and, once diagnosed, remain. A study on the age of onset of chronic diseases showed that the median age of onset for seven diseases (hypertension, diabetes, lung disease, heart disease or stroke, arthritis, neurological diseases, and cancer) was before age 60 [49]. Most new deficits added during follow-up were related to general health and functionality and were similar across the four frailty groups. Even when stratified by age groups, the same new deficits appeared in each age group within the

frailty levels. The new MEFI deficits, similar to risk factors found in the literature, included declines in mobility and stability (activity limitation, gait, muscular wasting, and falls), sensory impairment (hearing impairment and vision comorbidity), emotional problems (depression), memory and cognitive impairment, and other signs (sleep disturbance, incontinence). These are modifiable risk factors, and appropriate intervention programs may reduce deterioration. A primary carebased intervention found that a multifaceted approach (physical, nutritional, neurocognitive, and pharmacological) was effective in reversing frailty measures both short-term and at 18 months [50]. A systematic review showed that exercise training can reduce frailty levels and improve prognosis among older adults [51]. A meta-analysis of 15 studies found that resistance band exercise reduced frailty among older adults after 24 weeks [52]. Preventing frailty worsening is crucial due to its association with diseases. Progression from robust to frailty or pre-frailty increased the risk of new-onset diabetes [53] and incident cardiovascular diseases [54]. Moreover, patients who recovered to robust or pre-frail status had decreased risks of incident cardiovascular disease [54]. These findings suggest that reducing frailty has a further impact on reducing adverse outcomes.

The strength of our study lies in its large populationbased design with real-world data, exploring how frailty status changes over time, an issue that remains largely unexplored. To our knowledge, this study is the first to specify which deficits may appear first in terms of EFI deficits. In many health systems, these EFI deficits are documented, enabling easy routinely ongoing monitoring. Longitudinal frailty information at the population level is needed to plan services [45]. Specifically, identifying demographic and health risk groups will allow us to determine whom to intervene with first, and identifying deficits at risk for deterioration will help us focus on preventing or delaying frailty transition.

As an HMO, one of our roles is to prevent diseases and improve the health of our patients. Among the population aged 65+, it is essential to understand how modifiable risk factors such as sensory, functional, emotional, and cognitive factors impact frailty worsening, which in turn affects adverse outcomes. Focusing on intervention programs that address these health promotion issues can significantly contribute to disease control and slow the progression of frailty.

#### Limitation

One may argue that one year of follow-up is short. However, in high-aged individuals, a one-year observation period seemed sufficient to analyze frailty transition effectively [32]. Another limitation is the inherent limitations of administrative databases and the retrospective nature of this study, which may have led to the incorrect omission of certain deficits. As a result, there may be some random under-reporting, but this would be consistent across the two years compared. A third limitation concerns the length of the look-back period for chronic diseases (from age 55) compared to the commonly accepted one- to three-year period, which may have resulted in an overestimation of certain deficits. However, the decision to use a longer period was driven by coding practices and computational limitations in Meuhedet's EMR. Since chronic conditions often go uncoded in problem lists, a shorter look-back period could have led to the omission of various chronic conditions.

#### CONCLUSIONS

Frailty tends to worsen over time, but the process can be slowed with relevant prevention programs and treatment. Although chronic diseases in old age are frequent, they usually appear earlier in life, and new deficits that may appear later mainly include modifiable risk factors related to general health and functionality. Emphasizing intervention programs based on these health issues may significantly impact disease control and slow frailty worsening.

#### **MATERIALS AND METHODS**

In this study, we adhered to the STROBE reporting guideline for cohort studies [55].

#### Study design

This is a retrospective, longitudinal, population-based cohort study that includes repeated measures at baseline and one year later.

#### Setting

Healthcare in Israel is universal, and participation in a medical insurance plan is compulsory. All Israeli residents are entitled to basic health care as a fundamental right. The Israeli healthcare system is based on the National Health Insurance Law of 1995 [56], which mandates that all citizens residing in the country join one of four official health insurance organizations, all of which are run as not-for-profit organizations. The Meuhedet HMO is Israel's thirdlargest integrated healthcare service provider, serving over 1.3 million patients nationwide of all ages. Patient-level data are stored by Meuhedet in a comprehensive data warehouse, including chronic illnesses, community-care visits, medications, laboratory test results, pharmaceutical records, and sociodemographic information. The frailty level of all HMO members aged 65+ is updated each month based on the electronic medical record. The data for this study were extracted from the Meuhedet Electronic Health Record on 1 January 2023 and 1 January 2024 to enable oneyear follow-up.

#### Eligibility criteria

The cohort included all 119,952 Meuhedet members aged 65 years and over who were alive at the beginning of 2023, including 2,811 who died during 2023, excluding those who left the HMO during 2023. Housebound individuals were included, but patients living in an institution were excluded since most of the medical information is filed in the institution and not in the HMO. Specifically, for the analysis of what will worsen first, the 2,811 patients who died before the end of the year were excluded as the presence of new deficits could not be assessed.

#### Variables

#### **Predictors**

- Age groups: Age was divided into three categories: Young-old (65–74), middle-old (75–84), and oldestold (85+). These categories are common and are based on biological aspects of age.
- Sex: Males and females, as recorded in the electronic health record.
- Sector: About 75% of Israelis are Jews, and onequarter are Arabs, including Druze and Christian Arabs [57]. Among the Jewish population, about 17% are considered ultra-orthodox. Since the individual sector characteristic is not documented in the medical file, the sector used here is determined according to the clinic's sector where the patient belongs, namely, the Jewish secular, the Jewish Orthodox, and the Arabic sectors. Since most of the clinics are located in neighborhoods mostly composed of members of only one sector, this method allows for adequate classification.
- Socio-economic status (SES): Derived from the individual's home address and based on characteristics routinely collected by the Central Bureau of Statistics, ranging from 1 to 10. SES was grouped into three levels: 1–4 low, 5–7 medium, and 8–10 high.
- MEFI: MEFI, which stands for Meuhedet Electronic Frailty Index, is an EFI version we developed [6], based on Clegg [12] and on Orkaby Electronic Frailty Index [8]. MEFI is computed by extracting routinely collected health data directly from electronic medical records. It summarizes the number of deficits from a list of 36 variables,

including chronic diseases, basic and instrumental activities of daily living, social aspects, mood, hearing or vision impairment, and cognitive functioning (see Table 1). The weight was the same for all the deficits, one point, conforming to Clegg's definition. The look-back period for chronic diseases was from the age of 55, and the look-back period for non-disease deficits (such as functional deficits) was reduced to one year, a period that is well-accepted in the literature. Except for chronic diseases, a deficit that didn't appear anymore in the electronic health record was considered to reflect recovery or resolution of the condition. This assumption is justified by the fact that the health system in Israel allows access to primary care at almost no cost, and indeed, only 2.3% did not visit any medical staff during the look-back period. The MEFI classifies individuals as 'fit' or exhibiting frailty in the 'mild', 'moderate', or 'severe' frailty range, based on the MEFI score (fit (0-0.12; 0-4 deficits), mild (0.13-0.24; 5-8 deficits), moderate (0.25-0.36; 8-12 deficits), and severe (>0.36; 13+ deficits), in line with EFI categories described in the literature [12, 14]. MEFI was shown to predict mortality and hospitalization [6]. More details of the validation study have been described elsewhere [6].

- CCI: The Charlson Comorbidity Index (CCI) assesses comorbidity levels by considering both the number and severity of 17 pre-defined comorbid conditions [58]. The higher the score, the higher the predicted mortality rate. CCI was categorized into four grades: no comorbidity (0), mild (1–2), moderate (3–5), and severe (6+). Five CCI comorbidities out of 19 were common to both CCI and MEFI.
- BMI: The BMI is based on the last height and weight measures recorded in the electronic health record in the HMO. It was categorized into four levels according to the division mostly used in health: underweight less than 18.5, normal 18.5–<25, overweight 25–<30, and obese 30+.
- Hospitalization in the past year: This variable receives a value of 1 if the patient experienced any hospitalization in 2022, the year just preceding the follow-up period.

#### **Outcome measure**

The frailty index is calculated every month. Worsening was defined as any change to a worse frailty category one year following diagnosis. The worsening outcome received a value of 1 if the MEFI level on 1 January 2024, as divided into four categories, was worse than the MEFI level on 1 January 2023. Those who passed away during 2023 received a value of 1, which is considered worsening.

For determining what worsened first, the new deficit measure received a value of 1 if the deficit didn't appear in 2023 and appeared in 2024.

#### Statistical methods

Descriptive statistics of the population were presented as either means (standard deviations) for continuous variables or percentages for categorical variables. Worsening was presented by percentages, overall, and stratified by MEFI. Comparing worsening by demographic and clinical characteristics was tested using the chi-square test. Additionally, multivariable logistic regression was conducted to identify variables associated with frailty worsening, and a concordance index (C-Index) was used for model validation. Multicollinearity was tested by calculating variance inflation factors (VIFs). The percentage of new deficits among those still alive at the end of the follow-up was presented as a percentage and sorted by decreasing size in each frailty group. Data were analyzed using IBM SPSS statistics software [59]. All statistical tests were two-sided, and *p*-values lower than 0.05 were considered statistically significant.

### Abbreviations

HMO: Health Maintenance Organization; EFI: Electronic Frailty Index; MEFI: Meuhedet Electronic Frailty Index; EMR: Electronic Medical Record; SES: Socio-Economic Status; CCI: Charlson Comorbidity Index; BMI: Body Mass Index; aOR: adjusted Odd Ratio.

### **AUTHOR CONTRIBUTIONS**

FH designed the methodology, drafted the paper, calculated the MEFI, and performed the statistical analysis. YK initiated the development of a frailty index and supervised the whole process. ML revised and adapted the ICD-9 medical coding to Meuhedet's data. BM extracted the data from the EMR. IW, the geriatric nurse, and GS, the geriatric doctor, accompanied the process. FH, RS, YK, OS, AB, GS and IW participated in the development of the index. TS advised as a biostatistical consultant. YK, RS, and ML revised the manuscript for important intellectual content. DA, chief medical officer, contributed his knowledge at all stages.

### ACKNOWLEDGMENTS

Thanks to the many people who participated in our brainstorming meetings and contributed insights, including experts in geriatrics, health professionals and health teams in the field.

### **CONFLICTS OF INTEREST**

No sponsor had a role in the decision to undertake these analyses or to submit the study for publication. Each author asserts no proprietary interest in the result and no financial conflict of interest.

### ETHICAL STATEMENT AND CONSENT

In this study, were adhered to the STROBE reporting guideline for cohort studies. Due to the retrospective cohort design of this study, formal ethical approval and individual consent were not deemed necessary.

#### FUNDING

No funding was used for this paper.

#### **REFERENCES**

- Mitnitski A, Rockwood K. Aging as a process of deficit accumulation: its utility and origin. Interdiscip Top Gerontol. 2015; 40:85–98. <u>https://doi.org/10.1159/000364933</u> PMID:25341515
- Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013; 381:752–62. <u>https://doi.org/10.1016/S0140-6736(12)62167-9</u> PMID:<u>23395245</u>
- Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA, and Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001; 56:M146–56. <u>https://doi.org/10.1093/gerona/56.3.m146</u> PMID:11253156
- Lin KP, Li HY, Chen JH, Lu FP, Wen CJ, Chou YC, Wu MC, Derrick Chan DC, Chen YM. Prediction of adverse health outcomes using an electronic frailty index among nonfrail and prefrail community elders. BMC Geriatr. 2023; 23:474. <u>https://doi.org/10.1186/s12877-023-04160-1</u> PMID:37550602
- Kojima G. Frailty as a predictor of hospitalisation among community-dwelling older people: a systematic review and meta-analysis. J Epidemiol Community Health. 2016; 70:722–9. <u>https://doi.org/10.1136/jech-2015-206978</u> PMID:<u>26933121</u>
- Hershkowitz Sikron F, Schenker R, Koom Y, Segal G, Shahar O, Wolf I, Mazengya B, Lewis M, Laxer I, Albukrek D. Development and validation of an

electronic frailty index in a national health maintenance organization. Aging (Albany NY). 2024; 16:13025–38. <u>https://doi.org/10.18632/aging.206141</u> PMID:39448091

- Kojima G, Iliffe S, Walters K. Frailty index as a predictor of mortality: a systematic review and metaanalysis. Age Ageing. 2018; 47:193–200. <u>https://doi.org/10.1093/ageing/afx162</u> PMID:29040347
- Orkaby AR, Nussbaum L, Ho YL, Gagnon D, Quach L, Ward R, Quaden R, Yaksic E, Harrington K, Paik JM, Kim DH, Wilson PW, Gaziano JM, et al. The Burden of Frailty Among U.S. Veterans and Its Association With Mortality, 2002-2012. J Gerontol A Biol Sci Med Sci. 2019; 74:1257–64. <u>https://doi.org/10.1093/gerona/gly232</u> PMID:30307533
- 9. Vermeiren S, Vella-Azzopardi R, Beckwée D, Habbig AK, Scafoglieri A, Jansen B, Bautmans I, and Gerontopole Brussels Study group. Frailty and the Prediction of Negative Health Outcomes: A Meta-Analysis. J Am Med Dir Assoc. 2016; 17:1163.e1–17. <u>https://doi.org/10.1016/j.jamda.2016.09.010</u> PMID:<u>27886869</u>
- Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. ScientificWorldJournal. 2001; 1:323–36. <u>https://doi.org/10.1100/tsw.2001.58</u> PMID:<u>12806071</u>
- Rockwood K, Mitnitski A. Frailty in relation to the accumulation of deficits. J Gerontol A Biol Sci Med Sci. 2007; 62:722–7. <u>https://doi.org/10.1093/gerona/62.7.722</u> PMID:<u>17634318</u>
- Clegg A, Bates C, Young J, Ryan R, Nichols L, Ann Teale E, Mohammed MA, Parry J, Marshall T. Development and validation of an electronic frailty index using routine primary care electronic health record data. Age Ageing. 2016; 45:353–60. <u>https://doi.org/10.1093/ageing/afw039</u> PMID:<u>26944937</u>
- England NHS. National Health Service England. Identifying frailty. <u>https://www.england.nhs.uk/ourwork/clinical-policy/older-people/frailty/frailty-risk-identification/</u>. 2024.
- Lansbury LN, Roberts HC, Clift E, Herklots A, Robinson N, Sayer AA. Use of the electronic Frailty Index to identify vulnerable patients: a pilot study in primary care. Br J Gen Pract. 2017; 67:e751–6. <u>https://doi.org/10.3399/bjgp17X693089</u> PMID:<u>28947622</u>

- Mak JKL, Religa D, Jylhävä J. Automated frailty scores: towards clinical implementation. Aging (Albany NY). 2023; 15:4571–3. <u>https://doi.org/10.18632/aging.204815</u> PMID:37294544
- 16. Thandi M, Wong ST, Price M, Baumbusch J. Perspectives on the representation of frailty in the selectronic frailty index. BMC Prim Care. 2024; 25:4. <u>https://doi.org/10.1186/s12875-023-02225-z</u> PMID:<u>38166753</u>
- Pajewski NM, Lenoir K, Wells BJ, Williamson JD, Callahan KE. Frailty Screening Using the Electronic Health Record Within a Medicare Accountable Care Organization. J Gerontol A Biol Sci Med Sci. 2019; 74:1771–7. <u>https://doi.org/10.1093/gerona/glz017</u> PMID:30668637
- Abbasi M, Khera S, Dabravolskaj J, Vandermeer B, Theou O, Rolfson D, Clegg A. A cross-sectional study examining convergent validity of a frailty index based on electronic medical records in a Canadian primary care program. BMC Geriatr. 2019; 19:109. <u>https://doi.org/10.1186/s12877-019-1119-x</u> PMID:<u>30991943</u>
- Ambagtsheer RC, Beilby J, Dabravolskaj J, Abbasi M, Archibald MM, Dent E. Application of an electronic Frailty Index in Australian primary care: data quality and feasibility assessment. Aging Clin Exp Res. 2019; 31:653–60. <u>https://doi.org/10.1007/s40520-018-1023-9</u> PMID:<u>30132204</u>
- 20. Shen Y, Wang Y, Shi Q, Hou L, Chen X, Dong B, Hao Q. The Electronic Frailty Index is Associated with Increased Infection and All-Cause Mortality Among Older Patients with Primary Lung Cancer: A Cohort Study. Clin Interv Aging. 2021; 16:1825–33. <u>https://doi.org/10.2147/CIA.S335172</u> PMID:<u>34675497</u>
- 21. Nishimura S, Kumamaru H, Shoji S, Nakatani E, Yamamoto H, Ichihara N, Miyachi Y, Sandhu AT, Heidenreich PA, Yamauchi K, Watanabe M, Miyata H, Kohsaka S. Assessment of coding-based frailty algorithms for long-term outcome prediction among older people in community settings: a cohort study from the Shizuoka Kokuho Database. Age Ageing. 2022; 51:afac009. <u>https://doi.org/10.1093/ageing/afac009</u> PMID:35231096
- 22. Orfila F, Carrasco-Ribelles LA, Abellana R, Roso-Llorach A, Cegri F, Reyes C, Violán C. Validation of an electronic frailty index with electronic health records: eFRAGICAP index. BMC Geriatr. 2022; 22:404. <u>https://doi.org/10.1186/s12877-022-03090-8</u>

PMID:<u>35525922</u>

- Mak JKL, Hägg S, Eriksdotter M, Annetorp M, Kuja-Halkola R, Kananen L, Boström AM, Kivipelto M, Metzner C, Bäck Jerlardtz V, Engström M, Johnson P, Lundberg LG, et al. Development of an Electronic Frailty Index for Hospitalized Older Adults in Sweden. J Gerontol A Biol Sci Med Sci. 2022; 77:2311–9. https://doi.org/10.1093/gerona/glac069 PMID:35303746
- 24. Hollinghurst J, Fry R, Akbari A, Clegg A, Lyons RA, Watkins A, Rodgers SE. External validation of the electronic Frailty Index using the population of Wales within the Secure Anonymised Information Linkage Databank. Age Ageing. 2019; 48:922–6. <u>https://doi.org/10.1093/ageing/afz110</u> PMID:31566668
- Devereux N, Ellis G, Dobie L, Baughan P, Monaghan T. Testing a proactive approach to frailty identification: the electronic frailty index. BMJ Open Qual. 2019; 8:e000682. <u>https://doi.org/10.1136/bmjoq-2019-000682</u> PMID:<u>31523741</u>
- Setiati S, Laksmi PW, Aryana IGP, Sunarti S, Widajanti N, Dwipa L, Seto E, Istanti R, Ardian LJ, Chotimah SC. Frailty state among Indonesian elderly: prevalence, associated factors, and frailty state transition. BMC Geriatr. 2019; 19:182. https://doi.org/10.1186/s12877-019-1198-8 PMID:31269921
- Stolz E, Schultz A, Mayerl H, Roller-Wirnsberger R, Andrew C. Revisiting unstable disability and the fluctuations of frailty: a measurement burst approach. Age Ageing. 2024; 53:afae170. <u>https://doi.org/10.1093/ageing/afae170</u> PMID:<u>39113468</u>
- Bentur N, Sternberg SA, Shuldiner J. Frailty Transitions in Community Dwelling Older People. Isr Med Assoc J. 2016; 18:449–53. PMID:28471574
- 29. Wang MC, Li TC, Li Cl, Liu CS, Lin WY, Lin CH, Yang CW, Yang SY, Lin CC. Frailty, transition in frailty status and all-cause mortality in older adults of a Taichung community-based population. BMC Geriatr. 2019; 19:26.

https://doi.org/10.1186/s12877-019-1039-9 PMID:30691410

 Mian H, Wildes TM, Vij R, Pianko MJ, Major A, Fiala MA. Dynamic frailty risk assessment among older adults with multiple myeloma: A population-based cohort study. Blood Cancer J. 2023; 13:76. <u>https://doi.org/10.1038/s41408-023-00843-5</u> PMID:<u>37164972</u>

Kaskirbayeva D, West R, Jaafari H, King N, Howdon D, Shuweihdi F, Clegg A, Nikolova S. Progression of frailty as measured by a cumulative deficit index: A systematic review. Ageing Res Rev. 2023; 84:101789.

https://doi.org/10.1016/j.arr.2022.101789 PMID:<u>36396032</u>

- Kojima G, Taniguchi Y, Iliffe S, Jivraj S, Walters K. Transitions between frailty states among communitydwelling older people: A systematic review and metaanalysis. Ageing Res Rev. 2019; 50:81–8. <u>https://doi.org/10.1016/j.arr.2019.01.010</u> PMID:<u>30659942</u>
- 33. Thompson MQ, Theou O, Adams RJ, Tucker GR, Visvanathan R. Frailty state transitions and associated factors in South Australian older adults. Geriatr Gerontol Int. 2018; 18:1549–55. <u>https://doi.org/10.1111/ggi.13522</u> PMID:<u>30221449</u>
- 34. Elhussein L, Robinson DE, Delmestri A, Clegg A, Prieto-Alhambra D, Silman A, Strauss VY. Longitudinal trajectories of frailty are associated with short-term mortality in older people: a joint latent class models analysis using 2 UK primary care databases. J Clin Epidemiol. 2024; 173:111442. <u>https://doi.org/10.1016/j.jclinepi.2024.111442</u> PMID:<u>38942178</u>
- 35. Ye B, Chen H, Huang L, Ruan Y, Qi S, Guo Y, Huang Z, Sun S, Chen X, Shi Y, Gao J, Jiang Y. Changes in frailty among community-dwelling Chinese older adults and its predictors: evidence from a two-year longitudinal study. BMC Geriatr. 2020; 20:130. <u>https://doi.org/10.1186/s12877-020-01530-x</u> PMID:32272903
- 36. Mielke N, Schneider A, Huscher D, Ebert N, Schaeffner E. Gender differences in frailty transition and its prediction in community-dwelling old adults. Sci Rep. 2022; 12:7341. <u>https://doi.org/10.1038/s41598-022-11358-7</u> PMID:<u>35513428</u>
- Trevisan C, Veronese N, Maggi S, Baggio G, Toffanello ED, Zambon S, Sartori L, Musacchio E, Perissinotto E, Crepaldi G, Manzato E, Sergi G. Factors Influencing Transitions Between Frailty States in Elderly Adults: The Progetto Veneto Anziani Longitudinal Study. J Am Geriatr Soc. 2017; 65:179–84. <u>https://doi.org/10.1111/jgs.14515</u> PMID:27861714
- Liu Y, Huang L, Hu F, Zhang X. Investigating Frailty, Polypharmacy, Malnutrition, Chronic Conditions, and Quality of Life in Older Adults: Large Population-

Based Study. JMIR Public Health Surveill. 2024; 10:e50617. https://doi.org/10.2196/50617

PMID:39145920

- 39. Hwang AC, Lee WJ, Huang N, Chen LY, Peng LN, Lin MH, Chou YJ, Chen LK. Longitudinal changes of frailty in 8 years: comparisons between physical frailty and frailty index. BMC Geriatr. 2021; 21:726. <u>https://doi.org/10.1186/s12877-021-02665-1</u> PMID:34922488
- 40. Verghese J, Ayers E, Sathyan S, Lipton RB, Milman S, Barzilai N, Wang C. Trajectories of frailty in aging: Prospective cohort study. PLoS One. 2021; 16:e0253976. <u>https://doi.org/10.1371/journal.pone.0253976</u> PMID:34252094
- 41. Li CY, Al Snih S, Karmarkar A, Markides KS, Ottenbacher KJ. Early frailty transition predicts 15year mortality among nondisabled older Mexican Americans. Ann Epidemiol. 2018; 28:362–7.e3. https://doi.org/10.1016/j.annepidem.2018.03.021 PMID:29703521
- Barghouth MH, Klein J, Bothe T, Ebert N, Schaeffner E, Mielke N. Social support and frailty progression in community-dwelling older adults. Front Public Health. 2024; 12:1408641. <u>https://doi.org/10.3389/fpubh.2024.1408641</u> PMID:39086799
- 43. Sha S, Xu Y, Chen L. Loneliness as a risk factor for frailty transition among older Chinese people. BMC Geriatr. 2020; 20:300. <u>https://doi.org/10.1186/s12877-020-01714-5</u> PMID:32831020
- 44. Costenoble A, Knoop V, Debain A, Bautmans I, Van Laere S, Lieten S, Rossi G, Verté D, Gorus E, De Vriendt P, and Gerontopole Brussels Study Group. Transitions in robust and prefrail octogenarians after 1 year: the influence of activities of daily living, social participation, and psychological resilience on the frailty state. BMC Geriatr. 2023; 23:485. <u>https://doi.org/10.1186/s12877-023-04178-5</u> PMID:<u>37563561</u>
- 45. Walsh B, Fogg C, Harris S, Roderick P, de Lusignan S, England T, Clegg A, Brailsford S, Fraser SDS. Frailty transitions and prevalence in an ageing population: longitudinal analysis of primary care data from an open cohort of adults aged 50 and over in England, 2006-2017. Age Ageing. 2023; 52:afad058. <u>https://doi.org/10.1093/ageing/afad058</u> PMID:<u>37140052</u>
- 46. Nerobkova N, Park YS, Park EC, Shin J. Frailty transition and depression among community-

dwelling older adults: the Korean Longitudinal Study of Aging (2006-2020). BMC Geriatr. 2023; 23:148. <u>https://doi.org/10.1186/s12877-022-03570-x</u> PMID:<u>36932383</u>

- 47. Sheng K, Chen H, Qu X. The effects of cognitive leisure activities on frailty transitions in older adults in China:
  a CHARLS-Based longitudinal study. BMC Public Health. 2024; 24:1405.
  https://doi.org/10.1186/s12889-024-18889-w
  PMID:<u>38802740</u>
- 48. Cesari M, Gambassi G, van Kan GA, Vellas B. The frailty phenotype and the frailty index: different instruments for different purposes. Age Ageing. 2014; 43:10–2. <a href="https://doi.org/10.1093/ageing/aft160">https://doi.org/10.1093/ageing/aft160</a> PMID:24132852
- 49. Rashmi R, Mohanty SK. Examining chronic disease onset across varying age groups of Indian adults using competing risk analysis. Sci Rep. 2023; 13:5848. <u>https://doi.org/10.1038/s41598-023-32861-5</u> PMID:<u>37037884</u>
- 50. Romera-Liebana L, Orfila F, Segura JM, Real J, Fabra ML, Möller M, Lancho S, Ramirez A, Marti N, Cullell M, Bastida N, Martinez D, Giné M, et al. Effects of a Primary Care-Based Multifactorial Intervention on Physical and Cognitive Function in Frail, Elderly Individuals: A Randomized Controlled Trial. J Gerontol A Biol Sci Med Sci. 2018; 73:1688–74. https://doi.org/10.1093/gerona/glx259 PMID:29346524
- 51. Zhao W, Hu P, Sun W, Wu W, Zhang J, Deng H, Huang J, Ukawa S, Lu J, Tamakoshi A, Liu X. Effect of physical activity on the risk of frailty: A systematic review and meta-analysis. PLoS One. 2022; 17:e0278226. <u>https://doi.org/10.1371/journal.pone.0278226</u> PMID:<u>36454790</u>
- 52. Daryanti Saragih I, Yang YP, Saragih IS, Batubara SO, Lin CJ. Effects of resistance bands exercise for frail older adults: A systematic review and meta-analysis of randomised controlled studies. J Clin Nurs. 2022; 31:43–61.

https://doi.org/10.1111/jocn.15950 PMID:<u>34289511</u>

- 53. Zhang L, Chu C, Zhang Y, Wang M. Association of frailty index with new-onset diabetes: from the China Health and Retirement Longitudinal Study (CHARLS). Acta Diabetol. 2025. [Epub ahead of print]. <u>https://doi.org/10.1007/s00592-024-02441-8</u> PMID:<u>39760788</u>
- 54. He D, Wang Z, Li J, Yu K, He Y, He X, Liu Y, Li Y, Fu R, Zhou D, Zhu Y. Changes in frailty and incident cardiovascular disease in three prospective cohorts. Eur Heart J. 2024; 45:1058–68. <u>https://doi.org/10.1093/eurheartj/ehad885</u> PMID:<u>38241094</u>
- 55. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, and STROBE Initiative. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007; 335:806–8. <u>https://doi.org/10.1136/bmj.39335.541782.AD</u> PMID:<u>17947786</u>
- 56. State of Israel. State Health Insurance Act. https://natlex.ilo.org/dyn/natlex2/natlex2/files/down load/37205/IRL37205.pdf. 1994.
- 57. Israel Central Bureau of Statistics. Demographic characteristics definitions and explanations. <u>https://www.cbs.gov.il/en/subjects/Pages/Demograp hic-Characteristics.aspx</u>. 2024.
- 58. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40:373–83. <u>https://doi.org/10.1016/0021-9681(87)90171-8</u> PMID:3558716
- IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp See. <u>https://www.ibm.com/support/pages/how-cite-ibm-spss-statistics-or-earlier-versions-spss</u>.

# SUPPLEMENTARY MATERIALS

# **Supplementary Table**

# Supplementary Table 1. Top 15 deficits by MEFI and age groups.

	]	FIT	
All age groups	65–74	75–84	85+
30_Polypharmacy	30_Polypharmacy	30_Polypharmacy	18_Hearing
18_Hearing	18_Hearing	18_Hearing	16_Gait
16_Gait	26_MuscularWasting	16_Gait	30_Polypharmacy
26_MuscularWasting	16_Gait	26_MuscularWasting	20_Housebound
2_Anemia	2_Anemia	7_VisionComorbidity	26_MuscularWasting
7_VisionComorbidity	7_VisionComorbidity	2_Anemia	14_FallRelated
21_Hypertension	21_Hypertension	21_Hypertension	32_RequireForCare
33_Sleep disturbance	3_Anxiety	33_Sleep disturbance	1_ActLimitation
5_Arthritis	5_Arthritis	14_FallRelated	2_Anemia
3_Anxiety	33_Sleep disturbance	5_Arthritis	33_Sleep disturbance
15_Fatigue	15_Fatigue	22_Incontinence	7_VisionComorbidity
22_Incontinence	22_Incontinence	25_Memo_cog	34_SocialVulnerability
14_FallRelated	14_FallRelated	3_Anxiety	22_Incontinence
25_Memo_cog	36_WeightLoss	34_SocialVulnerability	15_Fatigue
36_WeightLoss	4_Depression	15_Fatigue	36_WeightLoss
	Μ	IILD	
All age groups	65–74	75–84	85+
30_Polypharmacy	30_Polypharmacy	30_Polypharmacy	30_Polypharmacy
18_Hearing	18_Hearing	18_Hearing	20_Housebound
16_Gait	16_Gait	16_Gait	18_Hearing
26_MuscularWasting	26_MuscularWasting	26_MuscularWasting	16_Gait
2_Anemia	2_Anemia	2_Anemia	26_MuscularWasting
33_Sleep disturbance	33_Sleep disturbance	33_Sleep disturbance	14_FallRelated
14_FallRelated	22_Incontinence	14_FallRelated	2_Anemia
22_Incontinence	3_Anxiety	22_Incontinence	1_ActLimitation
20_Housebound	14_FallRelated	20_Housebound	22_Incontinence
7_VisionComorbidity	7_VisionComorbidity	7_VisionComorbidity	33_Sleep disturbance
3_Anxiety	5_Arthritis	25_Memo_cog	25_Memo_cog
25_Memo_cog	15_Fatigue	3_Anxiety	7_VisionComorbidity
5_Arthritis	20_Housebound	15_Fatigue	34_SocialVulnerability
15_Fatigue	25_Memo_cog	1_ActLimitation	32_RequireForCare
4_Depression	21_Hypertension	34_SocialVulnerability	36_WeightLoss
	MOD	ERATE	
All age groups	65-74	75–84	85+
16_Gait	30_Polypharmacy	16_Gait	20_Housebound
30_Polypharmacy	16_Gait	26_MuscularWasting	16_Gait
26_MuscularWasting	26_MuscularWasting	30_Polypharmacy	26_MuscularWasting
18_Hearing	18_Hearing	18_Hearing	30_Polypharmacy

20_Housebound	2_Anemia	20_Housebound	18_Hearing
2_Anemia	22_Incontinence	2_Anemia	14_FallRelated
14_FallRelated	33_Sleep disturbance	14_FallRelated	2_Anemia
22_Incontinence	20_Housebound	22_Incontinence	1_ActLimitation
33_Sleep disturbance	14_FallRelated	33_Sleep disturbance	22_Incontinence
1_ActLimitation	4_Depression	1_ActLimitation	33_Sleepdisturbance
7_VisionComorbidity	1_ActLimitation	4_Depression	25_Memo_cog
4_Depression	7_VisionComorbidity	7_VisionComorbidity	7_VisionComorbidity
25_Memo_cog	3_Anxiety	25_Memo_cog	34_SocialVulnerability
3_Anxiety	15_Fatigue	3_Anxiety	4_Depression
36_WeightLoss	25_Memo_cog	36_WeightLoss	36_WeightLoss
	SE	VERE	
All age groups	65–74	75–84	85+
16_Gait	16_Gait	16_Gait	20_Housebound
20_Housebound	26_MuscularWasting	26_MuscularWasting	16_Gait
26_MuscularWasting	20_Housebound	20_Housebound	26_MuscularWasting
14_FallRelated	2_Anemia	2_Anemia	14_FallRelated
2_Anemia	14_FallRelated	14_FallRelated	2_Anemia
18_Hearing	21_Hypertension	22_Incontinence	18_Hearing
22_Incontinence	33_Sleep disturbance	18_Hearing	1_ActLimitation
1_ActLimitation	22_Incontinence	1_ActLimitation	33_Sleep disturbance
33_Sleep disturbance	18_Hearing	33_Sleep disturbance	22_Incontinence
4_Depression	1_ActLimitation	4_Depression	21_Hypertension
21_Hypertension	4_Depression	36_WeightLoss	34_SocialVulnerability
25_Memo_cog	3_Anxiety	3_Anxiety	7_VisionComorbidity
36_WeightLoss	25_Memo_cog	25_Memo_cog	25_Memo_cog
7_VisionComorbidity	7_VisionComorbidity	34_SocialVulnerability	36_WeightLoss
34_SocialVulnerability	15_Fatigue	7_VisionComorbidity	4_Depression