Study Report

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DARWIN EU® – Frailty and polypharmacy among adults with selected cancers at the time of diagnosis

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Contents

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Research question and objectives	The aim of this study was to estimate the prevalence of frailty and polypharmacy at the point of diagnosis of selected cancers in adults aged 18 and above and to describe their characteristics. The specific objectives of the study were: 1. To estimate the prevalence of frailty and polypharmacy in adults aged 18 and above diagnosed with selected cancers at the point of cancer diagnosis. 2. To describe the characteristics of adults aged 18 and above diagnosed with selected cancers among different frailty and polypharmacy categories at the point of cancer diagnosis.
Country(-ies) of study	Belgium, Estonia, Germany, Spain, The Netherlands, The United Kingdom
Author	Talita Duarte-Salles (tduarte@darwin-eu.org) Julieta Politi (j.politi@darwin-eu.org)

1. DESCRIPTION OF STUDY TEAM

Study team role	Names	Organisation
Study Project Manager/Principal Investigator	Talita Duarte-Salles Julieta Politi	Erasmus MC Erasmus MC
Data Scientist	Ross Williams Adam Black Maarten van Kessel Cesar Barbosa	Erasmus MC Erasmus MC Erasmus MC Erasmus MC
Epidemiologist	Julieta Politi	Erasmus MC
Clinical Domain Expert	Julieta Politi	Erasmus MC
Local Study Coordinator/Data Analyst	Cesar Mendosa Mees Mosseveld Laura Pérez Crespo Anna Palomar Lucía Amalia Carrasco Ribelles James Blash Antonella Delmestri Raivo Kolde Marek Oja	Erasmus MC – IPCI Erasmus MC – IPCI IDIAPJGol – SIDIAP IDIAPJGol – SIDIAP IDIAPJGol – SIDIAP IQVIA – DA Germany and LPD Belgium University of Oxford – CPRD-GOLD University Tartu – Estonian Biobank University Tartu – Estonian Biobank

2. DATA SOURCES

This study used routinely collected health data from 6 databases in the DARWIN EU network of data partners from 6 European countries. All databases were previously mapped to the OMOP CDM.

Data sources

1. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom
2. IQVIA Disease Analyzer Germany (IQVIA DA Germany), Germany
3. IQVIA Longitudinal Patient Database Belgium (IQVIA LPD Belgium), Belgium
4. Integrated Primary Care Information Project (IPCI), The Netherlands
5. Estonian Biobank (EBB), Estonia
6. Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP), Spain

3. ABSTRACT

Title

DARWIN EU® – Frailty and polypharmacy among adults with selected cancers at the time of diagnosis

Rationale and Background

Frailty, polypharmacy, and comorbidities are common and important factors which usually coexist in older patients. Assessment of frailty and polypharmacy is difficult due to lack of standardised definitions. However, accounting for them is relevant, especially among older adults with cancer, due to their adverse impact on cancer outcomes and treatment. Despite this, studies reporting on the prevalence of frailty and polypharmacy, specifically in older adults with cancer, remain sparse.

This study aimed to investigate the ability to characterise frailty and polypharmacy in real-world data sources, estimate the prevalence of frailty and polypharmacy in people aged 18 and above with selected cancers at the point of diagnosis, and describe their characteristics. While the focus was on older adults, this study explored the full age range of adulthood to contextualise the results better.

Research question and objectives

This study aimed to estimate the prevalence of frailty and polypharmacy at the point of diagnosis of selected cancers in adults aged 18 and above and describe their characteristics.

The specific objectives of the study were:

1. To estimate the prevalence of frailty and polypharmacy in adults aged 18 and above diagnosed with selected cancers at the point of cancer diagnosis.

2. To describe the characteristics of adults aged 18 and above diagnosed with selected cancers among different frailty and polypharmacy categories at the point of cancer diagnosis.

These objectives were analysed by database and selected cancer type, overall and stratified by age categories and sex.

Research Methods

Study design

Population-based cohort study.

Population

The study population included all individuals aged 18 years and above with a primary diagnosis of 10 selected cancers (lung, breast, ovary, endometrium, prostate, pancreas, colorectal cancer, lymphoma, leukaemia and myeloma) recorded between 01/01/2017 and 31/12/2022, with at least one year of prior history available before cancer diagnosis. Individuals with a diagnosis of cancer (any, excluding non-melanoma skin cancer) any time prior to the diagnosis of one of the selected cancers were excluded.

Additional eligibility of a minimum of one year of potential follow-up time prior to the end of last database observations was imposed for the estimation of one-year hospitalisation and mortality rates if the data sources capture this information.

Data sources

1. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom
2. IQVIA Disease Analyzer Germany (IQVIA DA Germany), Germany
3. IQVIA Longitudinal Patient Database Belgium (IQVIA LPD Belgium), Belgium
4. Integrated Primary Care Information Project (IPCI), The Netherlands
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6. Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP), Spain

Variables of interest

The number of prescriptions of different medications was calculated based on the overall number of different medicines prescribed during the 90 days prior to the index date (date of cancer diagnosis), and polypharmacy was measured as the maximum number of drug eras (i.e. a span of time when an individual is assumed to be exposed to a particular active ingredient) that overlap on any day during the 90-day period, dichotomised using two thresholds: the concomitant prescription of >= 5 and >= 10 medications (ingredient level) anytime during the 90 days prior to cancer diagnosis.

To measure frailty, a score was created based on the presence of polypharmacy (defined as >=5 prescriptions of medications as mentioned above) and the following 35 conditions included in frailty indexes previously proposed in the literature: mobility and transfer problems; housebound; activity limitation; visual impairment; hearing impairment; requirement for care; social vulnerability; falls; urinary incontinence; weight loss and anorexia; memory and cognitive problems; dizziness; dyspnoea; sleep disturbance; anaemia and haematinic deficiency; hypertension; ischaemic heart disease; heart failure; cerebrovascular disease; peripheral vascular disease; atrial fibrillation; heart valve disease; hypotension/syncope; diabetes; foot problems; arthritis; respiratory disease; peptic ulcer; thyroid disease; chronic kidney disease; osteoporosis; fragility fracture; Parkinsonism and tremor; urinary system disease; skin ulcer. In prior research, this definition was based on diagnosis codes recorded any time before or at cancer diagnosis, except for polypharmacy, for which we used the definition mentioned above (including medicine use 90 days before the index date). The frailty score was calculated based on the number of conditions present and polypharmacy (defined as >=5 concomitant prescriptions 90 days prior to index date) divided by the total number of conditions/polypharmacy mentioned above (35 conditions and 1 for polypharmacy prevalence). Individuals were then further categorised into the following levels of severity according to their scores: fit: 0–0.12; mild frailty: >0.12–0.24; moderate frailty= >0.24–0.36; severely frail: >=0.36. All co-morbidities and medications were used for large-scale patient characterisation, identified as concept/code and descendants.

Other variables of interest included the number of hospitalisations (SIDIAP and EBB) and mortality (CPRD GOLD, IPCI, EBB, SIDIAP) the year after the cancer diagnosis.

Sample size

No sample size was calculated as this was a descriptive Disease Epidemiology Study where we were interested in the characteristics of all incident cases of selected cancers.

Data analyses

The prevalence of frailty, overall and by categories (as defined based on the above-mentioned score), and polypharmacy (objective 1) were estimated at the time of cancer diagnosis.

Large-scale patient-level characterisation (objective 2) was conducted for individuals with different frailty and polypharmacy categories. Age and sex at the time of cancer diagnosis were described; Medical history was assessed for any time before the index date; up to 365 days before the index date; 365 to 31 days before the index date; 30 to 1 day before the index date; and at index date; Medication use history was

reported for 365 to 31 days before index date, for 30 to 1 day before index date, and at index date; hospitalisation and mortality rates were calculated for up to 365 days after index date.

For all analyses, absolute and relative frequencies were reported. A minimum cell counts of 5 was required when reporting results, and any smaller counts were reported as "<5" with zero counts reported as "0". Analyses were done separately for each database and selected cancers. Next to overall reporting, stratification by age category (18-44, 45-64, 65-74, 75-84 and 85+) and sex were conducted when possible (minimum cell count reached). Results for objective one, which estimated the prevalence of frailty in cancer patients, were further stratified by time period (before and after 2020).

Results

We described the prevalence of frailty and polypharmacy among 350,203 individuals aged 18 and above, with an incident cancer diagnosis among the 10 selected cancer types included in this study between 2017 and 2022, within the 6 participating databases (IQVIA DA Germany: 158,109; SIDIAP: 107,010; CPRD GOLD: 54,421; IPCI: 24,389; EBB: 3,310; IQVIA LPD Belgium: 2,964).

The median age ranged between 65 (EBB) and 69 years (IPCI, CPRD GOLD, IQVIA DA Germany, and IQVIA LPD Belgium). Overall, the sex distribution among cancer patients was similar across all databases and cancer types, with a slightly higher proportion of female cases among IPCI, CPRD GOLD, EBB, and IQVIA LPD Belgium.

The median frailty score ranged between 0.056 (IPCI & IQVIA DA Germany) and 0.139 (EBB). The prevalence of frailty (including all individuals with mild to severe frailty) ranged between 23.7% (IQVIA DA Germany) and 58.3% (EBB). Among the individual frailty categories, most individuals included in this study were classified as fit, with a prevalence ranging across databases between 41.7% in EBB and 76.3% in IQVIA DA Germany. Across all databases, the proportion of individuals across frailty categories decreased with increasing frailty severity. The prevalence of severe frailty was low and ranged between 0.2% (IQVIA LPD Belgium) and 5.0% (EBB).

The prevalence of polypharmacy using the >=5 threshold ranged between 19% (IQVIA DA Germany) and 56.2% (SIDIAP). The prevalence of polypharmacy decreased in all databases when the threshold increased to >=10 drugs, ranging from 4.3% (IQVIA DA Germany) to 22.9% in SIDIAP.

By individual cancer types, the highest prevalence of frailty was observed for pancreatic cancer, lung cancer, and multiple myeloma. These cancer types also showed the highest prevalence of polypharmacy in practically all databases.

<u>Prevalence of frailty conditions</u>

Some of the conditions included in the frailty score (excluding polypharmacy) returned zero counts. CPRD GOLD captured all conditions, followed by SIDIAP (only 1 condition with zero counts), while IPCI and IQVIA LPD Belgium were the databases with the highest number (6) of conditions with zero counts. The distribution of conditions varied by database, and some conditions showed marked differences in their prevalence across databases, such as fragility fracture, heart failure, and arthritis, among others. Among conditions reflecting disease state, foot problems returned zero counts in all databases, except CPRD GOLD. Among conditions reflecting symptoms and signs captured, falls also returned zero counts, except for CPRD GOLD, SIDIAP, and IQVIA LPD Belgium. Among conditions in the disability domain, housebound and requirement for care returned zero counts in more than one database (IPCI, EBB, IQVIA DA Germany, and IQVIA LPD Belgium for the former; and IPCI, EBB, and IQVIA LPD Belgium for the latter).

The 5 most prevalent conditions in each database were, in IPCI, chronic kidney disease (30.1%), hypertension (28.0%), urinary system disease (17.2%), visual impairment (15.7%), and respiratory disease (14.9%). For CPRD GOLD, chronic kidney disease (30.8%), hypertension (26.9%), Dyspnoea (21.7%),

respiratory disease (21.3%), and dizziness (13.4%). For SIDIAP, chronic kidney disease (45.8%), hypertension (44.3%), visual impairment (32.7%), urinary system disease (27.0%), and anaemia (24.0%). For EBB, chronic kidney disease (56.7%), hypertension (53.5%), respiratory disease (43.6%), arthritis (37.1%), and visual impairment (36.4%). For IQVIA DA Germany, hypertension (40.5%), chronic kidney disease (32.3%), respiratory disease (21.7%), thyroid disease (18.5%), and diabetes (14.2%). For IQVIA LPD Belgium, hypertension (50.8%), respiratory disease (33.6%), sleep disturbance (31.2%), chronic kidney disease (23.5%), and diabetes (15.6%).

Characteristics of Individuals by Frailty Category

Overall, there was no clear sex predominance among individuals considered fit. Mild frailty displayed some variation in sex predominance by database, while for moderate and severe frailty, there was a clear predominance of female sex in all databases. The proportion of women increased with increasing frailty severity. Regarding age, the proportion of older individuals increased with increasing frailty scores also in all databases.

Regarding polypharmacy (using the =>5 drugs threshold), among those classified as fit, the prevalence of polypharmacy was inconsistent among databases and ranged between 6.6% (IQVIA DA Germany) and 39.8% (CPRD GOLD). In the frail category, the prevalence of polypharmacy increased as frailty severity increased, and in the severe frailty category, polypharmacy was 89% and above. The prevalence of polypharmacy varied across databases. For example, mild frailty had a prevalence of polypharmacy between 45.7% in EBB and 86.9% in CPRD GOLD. However, for moderate frailty, the prevalence of polypharmacy was above 72% in all databases, and for severe frailty, it was consistently above 89%.

The prevalence of conditions included in the frailty score increased with increasing frailty severity category. Within the severe frailty category, some conditions reached a prevalence above 45% in all databases, such as chronic kidney disease (ranging between 90.1% in IPCI and 95.8% in EBB), hypertension (63.2% in CPRD GOLD to 96.3% in IQVIA DA Germany), and sleep disturbance (49% in SIDIAP to 85.5% in EBB) (Results on severe frailty in IQVIA LPD Belgium are not described because of low counts).

Characteristics of Individuals with Polypharmacy

Two thresholds of concomitant drug use were used to identify polypharmacy: >=5 and >=10 drugs. In terms of sex, there was a slight male predominance when the >=5 drugs threshold was used, while when using a >=10 drugs, there was a clear female predominance in some databases (IPCI, SIDIAP, and EBB, IQVIA LPD Belgium), while slight male predominance in the remaining (CPRD GOLD and IQVIA DA Germany). Regarding age, individuals with polypharmacy using the >=5 drugs threshold were generally within the 65-74 and 75-84 categories. Using the >=10 drugs polypharmacy threshold, most individuals were within the 75-84 and 85 and above category in almost all databases.

Within the >=5 drugs polypharmacy threshold, some conditions, such as chronic kidney disease, hypertension, and respiratory disease, had a prevalence of ~20% or above in all databases. Among the >=10 drugs polypharmacy category, the prevalence of conditions increased compared to >=5 drugs polypharmacy.

One-year hospitalisation rate and mortality risk by Frailty categories

The average number of hospitalisations ranged from fit to severely frail, between 1.18-1.54% in SIDIAP and 3.33-3.71% in EBB. SIDIAP had a clear positive gradient between hospitalisation rate and frailty and polypharmacy severity category.

Mortality data was only available for IPCI, CPRD GOLD, SIDIAP, and EBB. All databases exhibited a positive gradient between mortality risk and the increasing severity of frailty and polypharmacy. The one-year mortality risk ranged between 13-25% among fit individuals and 35-72% among severely frail individuals.

Large-scale characterisation by Polypharmacy and Frailty

The large-scale characterisation of conditions and drugs in this report was based on a window of 365-31 days before the index date (date of cancer diagnosis). Conditions related to hypertension, blood pressure findings, and heart disease were among the top 10 conditions in all databases. Respiratory system-related conditions, such as cough, Dyspnoea, and chronic obstructive respiratory disease, were also among the top 10 conditions.

Influenza and SARS-CoV-2 vaccination were among the 10 most common prescriptions in all databases, along with proton pump inhibitors, insulin sensitisers (metformin), blood pressure medications (calcium channel blockers, beta-blockers, diuretics), and analgesics (dipyrone and acetaminophen), among others.

Frailty and Polypharmacy by age, with a focus on older adults (aged >=65)

Among all databases, among 65-and-over age groups, there was a male predominance until the 85 years and above age group, after which, for most databases, a female predominance was observed (except for IQVIA LPD Belgium). The proportion of individuals with frailty increased with age. Frailty (understood as mild, moderate, and severe categories combined) ranged between 22.6-70.2% among those aged 65-74, between 31.7-82.7% among those aged 75-84, and between 39.9-92.3% among those aged 85 and above.

With increasing age, the proportion of individuals with greater frailty severity increased within each database. However, increments differed in each database. In this sense, in IPCI, for example, moderate frailty was 1.8% in the 65-74 age group and increased to 7.0% in the 85 and above age group, while in EBB, moderate frailty was 20.5% in the 65-74 age group and increased to 41.5% in the 85 and above age group. Similarly, severe frailty went 0.2% to 2.2% in IPCI, and 1.8% to 19.1% in SIDIAP, between the 65-74 and 85 and above age groups.

We also observed that polypharmacy increased with age. Among those aged 65-74, polypharmacy (using the >=5 drugs threshold) ranged between 19.4-62.6%, between 25-79.4% in those 75-84, and between 38.0-85.6% in those 85 and above (among all databases, the lowest prevalence of polypharmacy was observed in IQVIA DA Germany, while the highest in SIDIAP).

One-year hospitalisation rate and mortality risk in older adults (aged >=65)

Within each age group, one-year hospitalisation increased with increasing severity of frailty and polypharmacy categories. However, within each frailty category, hospitalisation seemed to decrease with increasing age, in SIDIAP, while in EBB, there was no clear pattern.

In terms of one-year mortality, risks increased within each age group with increasing severity of frailty and polypharmacy categories. The one-year mortality among severely frail individuals was highest among those aged 85 and above, at 62-81%.

Frailty and Polypharmacy by sex

Across all databases, women had a lower median age than men. The median age for women ranged from 63 in EBB to 67 years in IPCI and CPRD GOLD. Among individual frailty categories, a slightly higher proportion of women was observed with increasing frailty severity. The prevalence of polypharmacy (>=5 threshold) was greater in men than women and ranged between 20.3% (IQVIA DA Germany) and 60.3% (SIDIAP) in men. However, the prevalence of polypharmacy using the >=10 threshold did not show a clear predominance by sex, except for IPCI, in which the prevalence was higher for men (16.3%) compared to women (13.0%).

The distribution of frailty conditions varied by sex: chronic kidney disease, fragility fracture, osteoporosis, and thyroid disease predominated in women, while cerebrovascular disease, hypertension, ischaemic heart disease, and peripheral vascular disease predominated in males.

The one-year hospitalisation rate was greater in males in SIDIAP, among the moderate and severe frailty categories, and polypharmacy (>=10 drugs). However, in EBB, the hospitalisation rate was higher among women for all categories compared to men, except for severe frailty, where it was greater for men. One-year mortality was generally greater in men throughout all categories and databases (except for the severe frailty category in CPRD GOLD, in which mortality was higher in women).

Frailty and Polypharmacy by Cancer type

Overall, the 4 most common cancer types in all databases were Breast, Colorectal, Prostate, and Lung cancer. Each cancer type showed distinct age and sex characteristics. Age-wise, among different cancer types and databases, individuals with breast cancer were generally younger, while Multiple Myeloma patients were generally older compared to other cancer types. In terms of median frailty score by cancer type, the cancers with the highest median frailty score were Lung cancer (0.09-0.18), Pancreatic cancer (0.09-0.18), and Multiple Myeloma (0.09-0.21).
The highest one-year hospitalisation rate was observed for pancreatic cancer in EBB. In SIDIAP, no clear predominance was noted. For mortality rate, pancreatic cancer and lung cancer exhibited the highest mortality rates, irrespective of frailty severity. Other cancers seemed to display a positive gradient with increasing frailty category.

Frailty and Polypharmacy by cancer type in older adults (aged >=65)

Like the overall population, the most prevalent cancer types among individuals aged 65 and above were breast, colorectal, prostate, and lung cancer. However, the most prevalent cancer type varied by database. Within each database, the prevalence of each cancer type showed variations compared to the overall population. Among the most prevalent cancer types, the prevalence of breast cancer decreased, while it increased for colorectal, prostate, and lung cancer. For the remaining cancer types, variations were more modest.

In terms of median frailty score by cancer type in individuals 65 and above, the score generally increased with age for most cancer types and databases. The highest median frailty score observed was ovarian cancer in EBB among the 85 and above age group, followed by leukaemia, at 0.31, also in EBB.

The proportion of frailty categories (fit, mild, moderate, and severe) by cancer type varied with age. The highest prevalence of frailty by cancer type varied with age and database, and differences between cancer types were less marked compared to the overall population. In the 65-74 age group, the proportion of fit individuals was approximately 50% or higher in almost all cancer types and databases (except EBB, in which it was lower). With increasing age, the proportion of fit individuals decreased in all databases and, in most cases, was below 50%. Conversely, the highest proportion of severely frail individuals was among the 85 and above age group and was highest in SIDIAP. In EBB and IQVIA LPD Belgium, not all cancer types had counts in the 85 and above age category.

Polypharmacy, using the >= 5 drugs threshold, was highly prevalent among adults aged 65 and above. In the 65-74 age group, it was approximately 50% or above in almost all databases (except IQVIA Germany, where it was lowest). With increasing age, polypharmacy increased consistently among most cancer types in CPRD GOLD, IPCI, and SIDIAP, while the prevalence of polypharmacy in some cancer types varied slightly with age. Among the 85 and above group, no polypharmacy (>=10 drugs) was observed in EBB, as well as for some cancer types in IQVIA LPD Belgium, while the prevalence of polypharmacy using both >= 5 and >=10 thresholds was lowest among all cancer types in IQVIA DA Germany.

In terms of the distribution of frailty conditions by frailty category and solid cancer type (breast, colorectal, endometrial, lung, ovarian, pancreatic and prostate) in individuals aged 65-74, 75-84, and over 85, for practically all cancer types and databases, the prevalence of frailty conditions among fit cancer patients was below 50% in the 65-74 age group, while some conditions were over 50% in the 75-84 and 85 and

above age groups. Similar to the overall population, the prevalence of conditions gradually increased their proportion, as frailty increased, with increasing age, representing an increasing prevalence of each condition by cancer type as the frailty category progressed in practically all databases (except for severe frailty in IQVIA LPD Belgium, where counts were too low to graph). As observed in the overall population, some conditions were over 90% for some cancer types in individuals with severe frailty in all 3 age groups, such as chronic kidney disease, hypertension, and visual impairment.

One-year hospitalisation and mortality by cancer type in older adults (aged >=65)

The highest one-year hospitalisation rate in older adults (aged >=65) was observed for pancreatic cancer and lymphoma in EBB, which was highest in the 65-74 age group. In SIDIAP, no clear predominance was noted, and hospitalisation decreased with age. Regarding mortality risk in older adults (aged >=65), pancreatic cancer and lung cancer exhibited the highest mortality risks, irrespective of frailty severity and age. Ovarian cancer had very similarly high one-year mortality in the 85 and above age group. Within each frailty category and cancer type, mortality increased with age. There was no clear positive gradient with the increasing frailty category with each age category.

Discussion

We estimated the prevalence of frailty and polypharmacy among 350,203 individuals aged 18 and above (of which 66% were older adults, aged >=65 years) with incident-selected cancer types, diagnosed between 2017 and 2022 within the 6 participating databases, using routinely gathered EHR data on 35 conditions, disabilities, and signs and symptoms, together with polypharmacy, as proposed in prior EHR indexes. The prevalence of frailty (including all individuals with mild to severe frailty) ranged between 23.7% (IQVIA DA Germany) and 58.3% (EBB) and increased with age. Among older adults (aged >=65 and above), frailty (understood as mild, moderate, and severe categories combined) ranged between 22.6-70.2% among those aged 65-74, between 31.7-82.7% among those aged 75-84, and between 39.9-92.3% among those aged 85 and above.

The prevalence of polypharmacy (using the >=5 drugs threshold) ranged between 19% and 56.2% and also increased with age. Specifically, among those aged 65-74, polypharmacy ranged between 19.4-62.6%, while in those 75-84 it ranged between 25-79.4% and in those 85 and above, between 38-85.6% (among all databases, the lowest prevalence of polypharmacy was observed in IQVIA DA Germany, while the highest was SIDIAP).

Overall, the most prevalent condition identified within the study population was chronic kidney disease, and its prevalence increased with increasing frailty, reaching a prevalence of 90.1%-95.8% among those severely frail.

In the overall population, the one-year hospitalisation and mortality showed a positive gradient with increasing frailty severity. The one-year mortality among severely frail individuals was high, at 35-72%. Among older adults (aged >=65), one-year hospitalisation and mortality showed a positive gradient with increasing frailty severity and age. The one-year mortality among severely frail individuals was highest among those aged 85 and above, at 62-81%.

Our estimates underscore a high prevalence of frailty among cancer patients, which is at least doubled that of the general population (estimated at 10% in individuals 65 and above). Additionally, our results are consistent with prior frailty estimates among cancer patients. Furthermore, the gradient observed between the frailty categories and the hospitalisation and mortality outcomes is compatible with the performance of the electronic frailty indexes on which our score was based and similar to what has been described with Clinical Frailty Scores, which reassures that frailty seems identifiable by our approach. Still, our results displayed some heterogeneity across databases, most likely related to data capture, suggesting that frailty scores from some sources may be conservative. Regardless, frailty index scores have the potential to be

measured in some real-world data (RWD) datasets, and this approach could potentially be applicable to medicine evaluations or other areas if it is needed. While further work to optimise phenotype and assess its performance in other databases may be needed for optimal applicability, these findings suggest that despite the current limitations, the frailty score we implemented may provide meaningful insights.

4. LIST OF ABBREVIATIONS

Abbreviation	Name
ALL	Acute Lymphocytic Leukaemia
AML	Acute Myeloid Leukaemia
CDM	Common Data Model
CLL	Chronic Lymphocytic Leukaemia
CML	Chronic Myeloid Leukaemia
CPRD	Clinical Practice Research Datalink
DA	Disease Analyzer
DARWIN EU®	Data Analysis and Real-World Interrogation Network
DOI	Declaration Of Interests
DQD	Data Quality Dashboard
GP	General Practitioner
EHR	Electronic Health Record
EMA	European Medicines Agency
EBB	Estonian Biobank
ECOG	Eastern Cooperative Oncology Group
EGCUT	Estonian Genome Center at the University of Tartu
IPCI	Integrated Primary Care Information Project
LPD	Longitudinal Patient Database
NSCLC	Non-Small Cell Lung Cancer
PCT	Primary Care Teams
OMOP	Observational Medical Outcomes Partnership
RWD	Real-world data
SIDIAP	Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària
SNOMED	Systematised Nomenclature of Medicine
WHO	World Health Organisation

5. AMENDMENTS AND UPDATES

None.

6. MILESTONES

STUDY SPECIFIC DELIVERABLE	TIMELINE (planned)	TIMELINES (actual)
Draft Study Protocol	26/01/2024	
Final Study Protocol	February 2024	March 2024
Creation of Analytical code	March 2024	March 2024
Execution of Analytical Code on the data	March 2024	April 2024
Interim Study Report (if applicable)	N/A	N/A
Draft Study Report	April 2024	May 24th, 2024
Final Study Report	April/May 2024	
Draft Manuscript (if agreed on)		
Final Manuscript (if agreed on)		

7. RATIONALE AND BACKGROUND

Frailty, polypharmacy, and comorbidities are important considerations for the health of people aged ≥ 65 years. Frailty is an age-associated clinical syndrome characterised by decreased physiological reserves, increased vulnerability to stressors, and diminished capacity to maintain homeostasis due to a cumulative decline in the individuals' physiological systems (1). The estimated pooled prevalence of frailty among older adults (≥ 65) within European community settings is 12%(2). Despite being commonly observed in older adults and being associated with increased risks of adverse outcomes, including treatment toxicity, hospitalisation, and mortality, achieving a concise definition remains challenging(3). In addition to frailty, polypharmacy poses a further challenge and is an increasing concern when treating older adults due to the potential contraindications and drug-drug interactions among treatments(4). While there is no universal definition of polypharmacy, one of the most widespread definitions refers to the presence of 5 or more medications, with extreme polypharmacy defined as the presence of 10 or more medications, and its prevalence ranges from 7-45% in community settings (5, 6).

Unlike younger patients with cancer, older adults are at increased risk from cancer treatment, especially among vulnerable older subjects, who are more susceptible to unfavourable health events and complications during the disease course. In turn, there is interest in measuring frailty among older adults with cancer since frailty can be understood as an ageing-associated vulnerability and has been recognised as an important factor that can interfere with achieving successful cancer treatment in patients of advanced age (7-12).

Integrating frailty assessments into cancer clinical trials allows for a more comprehensive evaluation of patient's health status and helps tailor treatment approaches to individual patients. Identifying frailty enables clinicians to recognise patients who may have a poorer prognosis for adverse outcomes occurrence and be at higher risk of treatment-related complications. Some indexes have been proposed to predict the risk of chemotherapy toxicity and survival among this specific patient population(13). However, most indexes have focused primarily on patients with solid tumours.

Moreover, frailty assessment can allow decision-makers to understand better the patient population participating in trials and potentially account for frailty-related factors when considering the evidence on treatment efficacy and safety. In this sense, clinical trial inclusion and exclusion criteria may lead to uncertainty related to the external validity of trial results to the general patient population (which includes individuals of varying ages and performance statuses).

Frailty is a multidimensional concept, including physical, psychological, and social constructs, best captured in the context of a geriatric assessment (14). Two methods to measure frailty are generally the most accepted approaches for identifying frailty in older adults (9, 10). The Fried phenotypic frailty approach defines frailty as a clinical syndrome in which three or more of the following criteria are present: unintentional weight loss (10 lbs. in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity (15). The index proposed by Rockwood et al. defines frailty as an accumulation of deficits, where an individual's health status can be quantified as a proportion of ageing-associated deficits using measures from comprehensive geriatric assessment (16). While the ECOG (Eastern Cooperative Oncology Group) performance status scale is often used in oncology trials to assess cancer patients' functional and overall health status, data on ECOG status may not be routinely collected in electronic health records or administrative databases. Furthermore, some have argued that ECOG status does not reliably capture the full extent of frailty and may be subjective, with marked interobserver variability (17).

Several other frailty measures have been developed and applied to healthcare databases to support clinical care and research. Examples include the electronic frailty index, the modified frailty index, the hospital frailty risk score, and the Faurot frailty index (3, 18-20).

Cancers such as those of the lung, breast, ovary, endometrium, prostate, pancreas, colorectal cancer, lymphoma, leukaemia and myeloma are more prevalent in older adults. Additionally, older adults undergoing cancer-related treatment are more likely to experience polypharmacy because they tend to have a greater number of underlying comorbidities requiring treatment, together with the need to prescribe additional cancer-related medications, including cancer therapy and supportive medications (21). Despite several adverse outcomes being linked to polypharmacy, studies of polypharmacy in older adults with cancer are limited (22, 23).

This study aimed to investigate the ability to measure frailty and polypharmacy in selected DARWIN EU data sources, estimate the prevalence of frailty and polypharmacy in adults with selected cancers at the point of diagnosis, and describe their characteristics.

8. RESEARCH QUESTION AND OBJECTIVES

The aim of this study was to estimate the prevalence of frailty and polypharmacy in adults at the point of diagnosis of selected cancers and to describe their characteristics.

The specific objectives of the study were:

1. To estimate the prevalence of frailty and polypharmacy in adults aged 18 and above diagnosed with selected cancers at the point of cancer diagnosis.

2. To describe the characteristics of adults aged 18 and above diagnosed with selected cancers among different frailty and polypharmacy categories at the point of cancer diagnosis.

While understanding frailty and polypharmacy in older adults (aged 65 years and over) remains a key focus, we also characterised younger adults with the selected cancers to contextualise the results. All results were reported by database and stratified by age and sex. The results were also available by each cancer type included in the study. Results for objective 1 were further stratified by study period (before or after 2020) to capture the potential impact of the COVID-19 pandemic on the prevalence of frailty and polypharmacy.

Table 1. Primary and secondary research questions and objective

Objective:	To estimate the prevalence of frailty and polypharmacy at the point of diagnosis of selected cancers in adults aged 18 and above and to describe their characteristics.
Hypothesis:	N/A
Population ***(mention key inclusion-exclusion criteria):***	The study population included all individuals aged 18 years and above with a primary diagnosis of any of the selected cancers (lung, breast, ovary, endometrium, prostate, pancreas, colorectal cancer, lymphoma, leukaemia and myeloma) recorded between 01/01/2017 and 31/12/2022, who had at least one year of prior history available before cancer diagnosis (index date). Individuals with a history of cancer (any, excluding non-melanoma skin cancer) prior to the diagnosis of one of the selected cancers were excluded. Additional eligibility of a minimum of one year of potential follow-up time prior to the end of last database availability were imposed for the estimation of one-year hospitalisation and mortality rates.
Exposure:	The number of concomitant prescriptions was calculated based on the overall number of prescriptions during the 90 days prior to index date, and polypharmacy was measured as the maximum number of drug eras that overlap on any day during the 90-day period. Polypharmacy was defined as the concomitant prescription of >= 5 and >= 10 medications (ingredient level) anytime during the year prior to cancer diagnosis. A frailty score was implemented based on the presence of polypharmacy (defined as >=5 prescriptions of medications as mentioned above) and the following conditions included in frailty indexes (i.e.: eFI or eFRAGICAP): Mobility and transfer problems; Housebound; Activity limitation; Visual impairment; Hearing impairment; Requirement for care; Social vulnerability; Falls; Urinary incontinence; Weight loss and anorexia; Memory and cognitive problems; Dizziness; Dyspnoea; Sleep disturbance; Anaemia and haematinic deficiency; Hypertension; Ischaemic heart disease; Heart failure; Cerebrovascular disease; Peripheral vascular disease; Atrial fibrillation; Heart valve disease; Hypotension/syncope; Diabetes; Foot problems; Arthritis; Respiratory disease; Peptic ulcer; Thyroid disease; Chronic kidney disease; Osteoporosis; Fragility fracture; Parkinsonism and tremor; Urinary system disease; Skin ulcer. Their definition was based on diagnosis codes recorded any time prior or at cancer diagnosis. The score was calculated based on the number of present

	conditions and polypharmacy divided by the total number of conditions/polypharmacy mentioned above (35 conditions and 1 for polypharmacy prevalence) and was further categorised accordingly into the following levels of severity: fit: 0–0.12; mild frailty: >0.12–0.24; moderate frailty= >0.24–0.36; severely frail: >=0.36.
Comparator:	N/A
Outcome:	N/A
Time *(when follow up begins and ends):*	For the estimation of one-year hospitalization and mortality rates, follow-up start date was considered from date of cancer diagnosis (index date) until the earliest occurrence of the following: 1) loss to follow-up, 2) end of data availability, 3) date of death, or 4) end of the 365 days follow-up.
Setting:	Outpatient setting from 6 databases currently in DARWIN EU covering 6 European countries.
Main measure of effect:	Proportions

9. RESEARCH METHODS

9.1 Study Type and Study Design

This population-level descriptive epidemiology and patient-level characterisation study was classified as "off-the-shelf," as described in the DARWIN EU® Complete Catalogue of Standard Data Analyses (**Table 1**). It was a population-based cohort study on all incident cases of selected cancers.

Table 1. Description of Potential Study Types and Related Study Designs

STUDY TYPE	STUDY DESIGN	STUDY CLASSIFICATION
Population-level descriptive epidemiology	Population-level cohort	Off the shelf
Patient-level characterisation	Cohort analysis.	Off the shelf

9.2 Study Setting and Data Sources

This study used routinely collected health data from 6 databases in the DARWIN EU network of data partners from 6 European countries. All databases were previously mapped to the OMOP CDM.

Data sources

1. Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom
2. IQVIA Disease Analyzer Germany (IQVIA DA Germany), Germany
3. IQVIA Longitudinal Patient Database Belgium (IQVIA LPD Belgium), Belgium
4. Integrated Primary Care Information Project (IPCI), The Netherlands
5. Estonian Biobank (EBB), Estonia
6. Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària (SIDIAP), Spain

These databases fulfil the criteria required for a population- and patient-level characterisation study, allowing for large-scale characterisation while covering different regions of Europe. The selection of

databases was based on the availability of prior history data on conditions and medicines at the index date to estimate frailty and polypharmacy and perform patient-level characterisation. Detailed information on the selected data sources is described in **Table 2.**

The process of data accrual for each database is outlined individually in each of the following database-specific paragraphs. In relation to cancer diagnosis, some databases (SIDIAP, IQVIA DA Germany, and CPRD GOLD) have evaluated aspects such as accuracy, completeness, and timeliness of data, demonstrating high diagnostic sensitivity and responsiveness (24-26). One data source (EBB) is linked to the national cancer registry. Furthermore, databases have exhibited strong performance in identifying chronic diseases and prescribing medications and have been used in drug utilisation and epidemiological studies (25, 27-31). Regarding electronic frailty indexes, eFI has been previously used in CPRD GOLD (32), while eFRAGICAP has been developed and validated in SIDIAP (33). Additionally, two databases (EBB and SIDIAP) are connected to hospital discharge data, enabling the identification of hospitalisations. Last, four databases (EBB, SIDIAP, CPRD, IPCI) capture date of death.

Table 2. Description of the selected Data Sources

Country	Name of Database	Justification for Inclusion	Health Care setting	Type of Data	Number of active subjects	Calendar period covered by each data source	Ability to answer study objectives
BE	IQVIA LPD Belgium	Covers primary care setting with information on cancer diagnoses and medical history. Hospitalisations and deaths are not routinely recorded.	Primary care	EHR	1.1 million	31/12/2023	Objective 1 (without hospitalisation and mortality), Objective 2
DE	IQVIA DA Germany	Covers primary care setting with information on cancer diagnoses and medical history. Hospitalisations and deaths are not routinely recorded.	Primary care and outpatient specialist care	EHR	42 million	30/09/2023	Objective 1 (without hospitalisation and mortality), Objective 2

Country	Name of Database	Justification for Inclusion	Health Care setting	Type of Data	Number of active subjects	Calendar period covered by each data source	Ability to answer study objectives
ES	SIDIAP	Covers primary care setting, data on cancer diagnoses previously validated, information available on history of conditions and medications, number of hospitalisations and date of death.	Primary care with hospital data linkage	EHR	5.8 million	30/06/2023	Objectives 1 and 2
ET	EBB	Contains information on 200,000 participants with not only genetic information but also health insurance claims, digital prescriptions, discharge information and causes of death through linkage with the national death register. Data is linked to cancer registry.	Biobank with hospital and cancer registry linkage	Claims	0.2 million	01/06/2023	Objectives 1 and 2
NL	IPCI	Covers primary care setting, data on cancer diagnoses previously	Primary care	EHR	2.8 million	23/09/2023	Objective 1 (without hospitalisation), Objective 2

Country	Name of Database	Justification for Inclusion	Health Care setting	Type of Data	Number of active subjects	Calendar period covered by each data source	Ability to answer study objectives
		validated, information available on history of conditions and medications, and date of death. Hospitalisations are not routinely recorded.					
UK	CPRD GOLD	Covers primary care setting, data on cancer diagnoses, information available on history of conditions and medications, and date of death. Hospitalisations are not routinely recorded in the primary care data.	Primary care	EHR	17.3 million	01/01/2024	Objective 1 (without hospitalisation), Objective 2

BE = Belgium, CPRD = Clinical Practice Research Datalink, DA = Disease Analyzer; DE = Germany, EBB = Estonian Biobank, ES = Spain, ET = Estonia, IPCI = Integrated Primary Care Information Project, LPD = Longitudinal Patient Database; NL = The Netherlands, SIDIAP = Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària.

Clinical Practice Research Datalink (CPRD) GOLD, United Kingdom

The Clinical Practice Research Datalink (CPRD) GOLD is a database of anonymised electronic health records (EHR) from General Practitioner (GP) clinics in the UK that use the Vision® software system for their management (29). The source population encompasses 98% of the UK, registered with GPs responsible for non-emergency care and referrals. Participating GPs provide CPRD EHR for all registered patients who did not specifically request to opt out of data sharing. Covering 4.6% of the current UK population, GOLD includes 4.9% of contributing GP practices, providing comprehensive information within its defined source population. GOLD contains data from all four UK constituent countries, and the current regional

distribution of its GP practices is 5.7% in England, 55.6% in Scotland, 28.4% in Wales, and 10.2% in Northern Ireland (May 2022).

GOLD data include patient's demographic, biological measurements, clinical symptoms and diagnoses, referrals to specialists/hospital and their outcomes, laboratory tests/results, and prescribed medications. GOLD has been assessed and found broadly representative of the UK general population in terms of age, gender, and ethnicity (29). GOLD has been widely used internationally for observational research to produce nearly 3,000 peer-reviewed publications, making GOLD the most influential UK clinical database so far (34-36).

Regarding quality checks, the data's integrity, structure, and format are reviewed. Collection-level validation ensures integrity by checking that data received from practices contain only expected data files and that all data elements are of the correct type, length, and format. Duplicate records are identified and removed (29). Transformation-level validation checks for referential integrity between records ensure that there are no orphan records included in the database (for example, that all event records link to a patient), while research-quality-level validation covers the actual content of the data. CPRD provides a patient-level data quality metric as a binary 'acceptability' flag (29). This is based on recording and internal consistency of key variables, including date of birth, practice registration date and transfer out date.

IQVIA Disease Analyser (DA) Germany, Germany

IQVIA Disease Analyzer (DA) Germany is a database of de-identified electronic medical records from Germany's specialised and general primary practices (GP) since 1992. This dataset encompasses approximately 3% of all outpatient practices within Germany, ensuring a substantial representation of the national healthcare landscape (25, 37). The sampling methods used for practice selection, considering physician's demographics, clinical speciality focus, community size category and federal state location, were instrumental in constructing a database that accurately mirrors the diverse spectrum of healthcare providers in the country (25). Consequently, data within the IQVIA DA Germany database has been demonstrated to represent general and specialised practices throughout Germany.

The database contains demographic records, basic medical data, disease diagnoses according to the International Classification of Diseases, 10th revision (ICD-10), and prescription records (37). While the database partly records information on deaths and procedures, it currently does not support linkage with external data sources, meaning death recording is not comprehensive and does not routinely contain hospitalisation data. Routine updates are conducted at regular intervals.

As previously demonstrated, IQVIA DA Germany is suitable for pharmacoepidemiologic and pharmacoeconomic studies (37-39). Data quality is assessed based on several criteria, including completeness of information and correctness (e.g., linkage between diagnosis and prescriptions).

IQVIA Longitudinal Patient Database (LPD) Belgium, Belgium

IQVIA Longitudinal Patient Data (LPD) Belgium is a database of pseudo-anonymised electronic medical records from general practices (GPs) in Belgium since 2005. The database encapsulates records of approximately 10% of the Belgian patient population.

This patient-level database captures patient demographics and diagnoses (using a specific diagnostic coding system that can be bridged with ICD-10-CM codes). In addition, it encompasses medical history, prescription data (associated with a hard-coded diagnosis), as well as supplementary metrics such as anthropometric measures (height, weight), vital signs (blood pressure) and results from laboratory tests (31), All patients and GPs in the database are pseudo-anonymised and can be followed longitudinally based on a unique identifier (ID). Strict attention to confidentiality is present at every stage of data collection, storage and analysis in accordance with GDPR and Belgian Ethics Committee recommendations. IQVIA LPD

Belgium database is nationally representative in terms of both geographical coverage and patient demographic characteristics, including age and sex (31).

This database has been widely used in previous drug utilisation and epidemiological studies and represents a robust source of information on primary care in Belgium (40-42). Date of death and hospitalisations are not available.

Estonian Biobank (EBB), Estonia

The Estonian Biobank (EBB) is a population-based biobank of the Estonian Genome Center at the University of Tartu (EGCUT), encompassing close to 20% of Estonia's adult population. The current biobank size reflects the age, sex, and geographical distribution of the adult Estonian population: Estonians represent 83%, Russians 14%, and other nationalities 3% of all participants.

All participants underwent a standardised health assessment, including providing blood samples for purification of DNA, white blood cells and plasma, and completed a questionnaire covering various health-related topics, such as lifestyle, diet and clinical diagnoses (30).Follow-up data are available via linkage with national health-related registries and re-examination of participants. Furthermore, electronic health records are updated every half year for phenotypic outcome information. The EBB database is regularly linked with national registries (such as Cancer Registry and Causes of Death Registry), hospital databases, and the national health insurance fund database, which holds treatment and service bills. Diseases and health problems are recorded as ICD-10 codes and prescribed medicine according to the ATC classification. As previously demonstrated, the Estonian Biobank has been suitable for epidemiological and pharmacogenetic studies (43-47).

Information System for Research in Primary Care (SIDIAP), Catalonia, Spain

The Information System for Research in Primary Care (SIDIAP) is a dynamic database of pseudo-anonymised electronic health records of Catalonia's (Spain) primary care patient population (24), It contains data on approximately 80% of the Catalan population registered in over 280 primary care practices throughout Catalonia since 2006.

The database contains data recorded in primary care centres daily. Additionally, it integrates data from external sources, including biomarkers data from laboratories and records of drug prescription and dispensation. The dataset covers demographics, all-cause mortality, disease diagnoses classified under the International Classification of Diseases 10th revision (ICD-10), prescription and dispensation records of drugs, laboratory test results, socio-economic indicators, vaccination records, lifestyle information, parent-child linkage and various clinical parameters. Additional data from other data sources, such as hospital discharges, mental health centres or specific disease registries, can be obtained through diverse linkages. The demographic composition within SIDIAP closely mirrors that of the broader Catalan population, encompassing a representative spectrum of geographic distribution, age, and sex proportions. The database is updated every 6 months.

SIDIAP data quality has been previously documented, and SIDIAP has proved valuable for epidemiological studies (39, 48-56). Regarding data integrity and reliability, SIDIAP has been subject to rigorous evaluation. Quality checks have been implemented, including central identification of duplicate patient IDs and visual inspection for temporal patterns in recording certain variables. Furthermore, the data undergoes assessment for availability (longitudinality and reliability), plausibility (range checks and unusual values) and consistency using visualisation tools. Specifically, for biochemistry data, consistency for measurements taken in different laboratories is assessed, and unit conversion is undertaken when needed.

Integrated Primary Care Information Project (IPCI), The Netherlands

The Integrated Primary Care Information (IPCI) database is a longitudinal observational database containing routinely collected data from computer-based patient records of a selected group of general practitioners (GPs) across the Netherlands (57). IPCI was started in 1992 by the Department of Medical Informatics of the Erasmus University Medical Center in Rotterdam. The current database includes patient records from 2006, when the size of the database started to increase significantly. The demographic composition of the IPCI population mirrors that of the general Dutch population in terms of age and sex. Although the geographical spread is limited, GP practices are in urban and non-urban areas.

Patient-level data includes demographic information, patient complaints and symptoms, diagnoses, laboratory test results, lifestyle factors and correspondence with secondary care, such as referral and discharge letters, which GPs record. Dutch GPs use the International Classification of Primary Care (ICPC-1) coding for complaints, symptoms and diagnoses, an international standard developed and updated by the World Organization of Family Doctors (WONCA) International Classification Committee.

IPCI data quality has been previously documented, and IPCI has proved valuable for epidemiological studies. Dates of birth and death are rounded to months (58-62). Extensive quality control steps are performed before each data release. These include comparisons of patient characteristics between practices and checks to identify abnormal temporal data patterns in practices. Additional checks include over 200 indicators related to population characteristics (e.g. reliability of birth and mortality rates) and medical data (e.g. availability of durations of prescriptions, completeness of laboratory results, availability of hospital letters and prescriptions, proportion of patients with blood pressure measurement, etc.) (57). Two quality scores have been created based on this information. Practices with low scores have been excluded.

The IPCI database is registered on the HMA-European Medicines Agency (EMA) Catalogues of real-world data sources (https://catalogues.ema.europa.eu/catalogue-rwd-sources; previously, ENCePP resources database). IPCI does not include linkage to hospitalisation data.

9.3 Study Period

The study period was between 01/01/2017 and 31/12/2022 for diagnosis of cancer and up to 31/12/2021 for estimation of hospitalisation rate and mortality risk (to allow sufficient time for one-year follow-up).

9.4 Follow-up

Subjects included in the study were followed up to one year from cancer diagnosis (index date) to estimate one-year hospitalisation rate and mortality risk. Subjects were followed up until the earliest of the following: 1) loss to follow-up, 2) end of data availability, 3) date of death, or 4) one year after index date.

9.5 Study Population, inclusion, and exclusion criteria

The study population for patient characterisation included all individuals aged 18 years and above with a primary diagnosis of one of the following 10 selected cancers:

- Lung
- Breast
- Ovary
- Endometrium
- Prostate
- Pancreas
- Colorectal cancer
- Lymphoma
- Leukaemia

- Multiple myeloma

recorded between 01/01/2017 and 31/12/2022, with at least one year of prior history available before cancer diagnosis (**Table 4, Table 4**). Individuals with a prior history of cancer (excluding non-melanoma skin cancer) at any time before the index date were excluded from the study (**Table 5**). Cancer cases were identified based on a recorded code indicating a diagnosis or observation for each specific cancer. Conditions in the OMOP CDM use the Systematised Nomenclature of Medicine (SNOMED) as the standard vocabulary for diagnosis codes. The list of codes included in each concept set used to identify each individual cancer type is provided in **Appendix I. Table 1**.

Additionally, a minimum of one year of potential follow-up time was imposed to estimate one-year hospitalisation rate and mortality risk, which was one year before the data lock date as described in **Table 2.**

Table 3. Operational definition of time 0 (index date) and other primary time anchors.

Study population name(s)	Time Anchor Description	Number of entries	Type of entry	Washout window	Care Setting[1]	Code Type	Diagnosis position	Incident with respect to…	Measurement characteristics/validation	Source of algorithm
All persons in each database eligible for the study	Date of selected cancer diagnosis	Single entry	Incident	Any time prior to cancer diagnosis	OP, OT	SNOMED	Any	Any cancer diagnosis except non-melanoma skin cancer	N/A	N/A

[1] OP = outpatient, OT = other, n/a = not applicable

Table 4. Operational definitions of inclusion criteria.

Criterion	Details	Order of application	Assessment window	Care Settings[1]	Code Type	Diagnosis position	Applied to study populations:	Measurement characteristics/validation	Source for algorithm
Prior database history of one year (objective 1)	Study participants were required to have a year of prior history observed before contributing observation time	After	one year	OP, OT	N/A	N/A	All study participants	N/A	N/A
Minimum potential follow-up time (only for calculation of one-year hospitalisation rate and mortality risk)	Only participants with a cancer diagnosis (index date) occurring one year prior to end of data availability in the database were included	After	one year	OP, OT	N/A	N/A	All study participants	N/A	N/A

[1] OP = outpatient, OT = other, n/a = not applicable

Table 5. Operational definitions of exclusion criteria.

Criterion	Details	Order of application	Assessment window	Care Settings[1]	Code Type	Diagnosis position[2]	Applied to study populations:	Measurement characteristics/ validation	Source for algorithm
History of cancer diagnosis	Participants with a diagnosis of cancer (any, excluding non-melanoma skin cancer) any time prior to the recorded code of the selected cancer or prior to the start of the study period	After	Any time prior to cancer diagnosis	OP, OT	SNOMED	Any	All study participants	N/A	N/A

[1] OP = outpatient, OT = other, n/a = not applicable

9.6 Variables

9.6.1 Exposure/s

The prevalence of polypharmacy and frailty was calculated by identifying prescriptions and coded selected conditions (**Table 6**).

Polypharmacy was identified by calculating the total number of concomitant prescriptions during the 90 days before the index date. Polypharmacy was measured as the maximum number of drug eras that overlap on any day during the 90-day period before the index date. Two thresholds were used to define polypharmacy, based on the simultaneous number of drugs during the 90-day period: the concomitant prescription of >= 5 and >= 10 medications (ingredient level) anytime during the 90 days before cancer diagnosis.

A frailty score was created, which included 36 items. Of the 36 items used to identify frailty, one was the presence of polypharmacy, defined as >=5 prescriptions of medications (as mentioned above). The following 35 components were based on conditions included in frailty indexes previously proposed in the literature (3, 33). We refer to these as "frailty conditions" throughout the text, although they represent disease states, symptoms/signs, and disabilities, as specified below:

Disease States

- Anaemia
- Arthritis
- Atrial fibrillation
- Chronic kidney disease
- Cerebrovascular disease
- Diabetes
- Foot problems
- Fragility fracture
- Heart failure
- Heart valve disease
- Hypertension
- Hypotension
- Ischaemic heart disease
- Osteoporosis
- Parkinsonism & tremor
- Peptic ulcer
- Peripheral vascular disease
- Respiratory disease
- Skin ulcer
- Thyroid disease
- Urinary system disease

Symptoms/signs

- Dyspnoea
- Dizziness
- Falls
- Memory & Cognitive problems
- Sleep disturbance
- Urinary incontinence
- Weight loss & anorexia

Disability

- Activity limitation
- Hearing impairment
- Housebound
- Mobility transfer
- Requiring care
- Social vulnerability
- Visual impairment

Each individual condition was defined based on SNOMED diagnosis codes recorded before or at cancer diagnosis. The final code list for conditions is provided in **Appendix I. Table 2.**

The score was calculated based on the number of present conditions (including polypharmacy) and divided by 36. The total number of conditions (including polypharmacy) was further categorised into the following levels of severity according to prior literature (3, 66):

- Fit: 0–0.12
- Mild frailty: >0.12–0.24
- Moderate frailty= >0.24–0.36
- Severely frail: >=0.36

Table 6. Operational Definitions of Exposure

Characteristic	Details	Type of variable	Assessment window	Care Settings[1]	Code Type	Diagnosis Position	Applied to study populations:	Measurement characteristics/validation	Source for algorithm
Polypharmacy	The concomitant prescription of >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period)	Counts	90 days prior to ID	OP, OT	RxNorm	N/A	All study participants	N/A	N/A
Score of frailty conditions	See description in section 8.6.1 above	Counts	Any time prior or at ID	OP, OT	SNOMED	N/A	All study participants	N/A	N/A

[1] ID = index date, P = outpatient, OT = other, n/a = not applicable

9.6.2 Outcome/s

Outcomes of interest included the number of hospitalisations and date of death during the year following the date of cancer diagnosis.

9.6.3 Other covariates, including confounders, effect modifiers and other variables

Age at cancer diagnosis was described. The following age groups were used: 18-44, 45-64, 65-74, 75-84 and 85 years and over. The sex (male/ female) of the study participants was also identified.

The following cancer sites were further categorised as follows:

- Lung cancer: NSCLC and all other lung cancers
- Leukaemia: Acute and Chronic Lymphocytic leukaemia (ALL and CLL, respectively) and Acute and Chronic myeloid leukaemia (AML and CML, respectively) were described individually.
- Lymphomas: Hodgkin and non-Hodgkin lymphoma.

All co-morbidities and medications were used for large-scale patient characterisation, identified as concept/code and descendants.

Table 7. Operational definitions of covariates.

Characteristic	Details	Type of variable	Assessment window	Care Settings[1]	Code Type	Diagnosis Position	Applied to study populations:	Measurement characteristics/valid	Source for algorithm
Co-morbidities	Large-scale patient-level characterisation regarding underlying comorbidities	Counts	At index date (ID), for 30 to 1 day before ID, for 365 to 31 days before ID, at any time and up to 366 days before ID	OP, OT	SNOMED	N/A	All study participants	N/A	N/A
Concomitant medication	Large-scale patient-level characterisation regarding use of concomitant drugs	Counts	At index date (ID), for 30 to 1 day before ID, for 365 to 31 days before ID, 1 to 30 post ID, 1 to 90 post ID, and 1 to 365 days post ID	OP, OT	RxNorm	N/A	All study participants	N/A	N/A
Hospitalisation and date of death	One-year hospitalization rate and mortality risk were calculated after ID	Counts	One-year post-index	OP, OT	N/A	N/A	All study participants	N/A	N/A

[1] ID = index date, P = outpatient, OT = other, n/a = not applicable

9.7 Study size

No sample size was calculated as this was a descriptive Disease Epidemiology Study where we were interested in the frailty, polypharmacy, and other demographic and clinical characteristics of all incident cases of selected cancers in each database.

9.8 Data transformation

Analyses were conducted separately for each database. Before the study initiation, quality control checks were performed, including analytical test runs. After all the tests were passed (see Section 11 Quality Control), the final package was released in the version-controlled Study Repository for execution against all the participating data sources.

The data partners locally executed the analytics against the OMOP-CDM in R Studio, reviewed, and approved the by default aggregated results before returning them to the Coordination Centre. Sometimes multiple execution iterations were performed, and additional fine tuning of the code base was needed.

The study results of all data sources were checked, after which they were made available to the team in the Digital Research Environment and the Dissemination Phase started. All results were locked and timestamped for reproducibility and transparency.

9.9 Statistical Methods

9.9.1 Main Statistical Methods

The type of analysis is described in **Table 8**.

Table 8. Description of study types and type of analysis.

STUDY TYPE	STUDY CLASSIFICATION	TYPE OF ANALYSIS
Population-level descriptive epidemiology	Off-the-shelf	- Prevalence rates of the condition of interest
Patient-level characterisation	Off-the-shelf	- large-scale characterisation - patient-level characteristics - Prognosis / progression to a pre-specified outcome

Data analyses

The prevalence of each component of the frailty score, frailty, frailty categories (based on the definition described in Section 8.6.1), and polypharmacy (objective 1) was estimated by database at the time of cancer diagnosis for each cancer type.

The hospitalisation rate was computed as the total number of hospitalisations within the year following the selected cancer diagnoses, divided by the total number of individuals within that category and period. Recurrent hospitalisations were observed for some subjects. Hence, a rate >1 indicates that the number of hospitalisations exceeded the number of individuals within that category. The mortality risk

was computed as the total number of deaths within the year following the selected cancer diagnosis, divided by the total number of individuals within that category and period. It is expressed as a percentage in text.

Large-scale patient-level characterisation (objective 2) was conducted for individuals with different frailty (fit, mild, moderate, severe frailty) and polypharmacy categories (no polypharmacy, >=5 medications, >=10 medications), characterising age and sex at the time of cancer diagnosis.

Medical history for patient-level characterisation was assessed anytime—and up to 365 days before the index date, for 365 to 31 days before the index date, for 30 to 1 day before the index date, and at the index date; medication use history was reported for 365 to 31 days before index date, for 30 to 1 day before index date, and at index date; hospitalisation rate and mortality risk were calculated for up to 365 days after index date.

For all analyses, absolute and relative frequencies were reported. Minimum cell counts of 5 were used when reporting results, and any smaller counts were reported as “<5”. Zero counts were reported as “0”.

Analyses were done separately for each database and selected cancer. In addition to overall reporting, stratification by age category (18-44, 45-64, 65-74, 75-84, and 85+ years) and sex was conducted when possible (minimum cell count reached).

Results for objective 1, estimating the prevalence of frailty in cancer patients, were further stratified by time period (before and after 2020) to capture the potential impact of the pandemic on the prevalence of frailty and polypharmacy.

9.9.3 Missing Values

Missing data

As stated in Section 8.4, subjects were followed up from the date of cancer diagnosis until the earliest of the following: 1) loss to follow-up, 2) end of data availability, 3) date of death, or 4) one year after index date.

Patients in 1) and 2) with missing part of their follow-up were censored at the time of loss to follow-up or end of data availability and that reported hospitalisation rate and mortality risk implicitly assume censoring occurs at random. Patients in 4) were administratively censored.

9.9.4 Sensitivity Analysis

N/A

10. DATA MANAGEMENT

10.1 Federated Network Analyses

Analyses were conducted separately for each database. Before study initiation, test runs of the analytics were performed on a subset of the data sources and a simulated set of patients and quality control checks were performed. Once all the tests were passed, the final package was released in the version-controlled Study Repository for execution against all the participating data sources.

The data partners locally executed the analytics against the OMOP-CDM in R Studio, reviewed and approved the default aggregated results, and returned them to the Coordination Centre. Multiple execution iterations were performed, and additional fine-tuning of the code base was needed. A service desk was available for support during the study's execution.

The study results of all data sources were checked, after which they were made available to the team in the Digital Research Environment (DRE) before starting the Study Dissemination Phase. All results were locked and timestamped for reproducibility and transparency.

10.2 Patient Privacy Protection

Cell suppression was applied as required by databases to protect personal privacy. Cell counts < 5 were masked.

10.3 Data management

All databases were mapped to the OMOP common data model. This enables the use of standardised analytics and tools across the network since the structure of the data and the terminology system are harmonised. The OMOP CDM is developed and maintained by the Observational Health Data Sciences and Informatics (OHDSI) initiative and is described in detail on the wiki page of the CDM: https://ohdsi.github.io/CommonDataModel and in The Book of OHDSI: http://book.ohdsi.org.

The analytic code for this study was written in R. Each data partner executed the study code against their database containing patient-level data and returned the results set, which only contained aggregated data. The results from each contributing data site were then combined in tables and figures for the study report.

10.4 Data storage and protection

For this study, participants from various EU member states processed personal data collected in national/regional electronic health record databases. Due to the sensitive nature of personal medical data, ethical and regulatory aspects were taken into account, and all reasonable measures to ensure compliance with ethical and regulatory issues regarding privacy protection.

All databases used in this study are regularly used for pharmaco-epidemiological research and have a well-developed mechanism to ensure adherence to European and local regulations regarding the ethical use of the data and adequate privacy control. In agreement with these regulations, rather than combining person-level data and performing only a central analysis, local analyses are run, which generate non-identifiable aggregate summary results.

The output files are stored in the DARWIN Digital Research Environment. These output files do not contain any data that allows the identification of subjects included in the study. The DRE implements further security measures to ensure a high level of stored data protection to comply with the local implementation of the General Data Protection Regulation (GDPR) (EU) 679/20161 in the various member states.

11. QUALITY CONTROL

General database quality control

Several open-source quality control mechanisms for the OMOP CDM have been developed (see Chapter 15 of The Book of OHDSI http://book.ohdsi.org/DataQuality.html). In particular, data partners have run the OHDSI Data Quality Dashboard tool (https://github.com/OHDSI/DataQualityDashboard). This tool provides numerous checks on the mapped data's conformance, completeness and plausibility. Conformance focuses on checks that describe the compliance of the representation of data against internal or external formatting, relational, or computational definitions, completeness in the sense of data quality is solely focused on quantifying missingness, or the absence of data, while plausibility seeks to determine the believability or truthfulness of data values. Each category has one or more subcategories and is evaluated in two contexts: validation and verification. Validation relates to how well data align with external benchmarks with expectations derived from known true standards, while verification relates to how well data conform to local knowledge, metadata descriptions, and system assumptions.

Study-specific quality control

When defining specific cancers and co-morbidities, a systematic search of possible codes for inclusion was previously identified using the CodelistGenerator R package (https://github.com/darwin-eu/CodelistGenerator). This software allows the user to define a search strategy to query the vocabulary tables of the OMOP CDM to find potentially relevant codes. The codes returned were then reviewed to consider their relevance. In addition, the CohortDiagnostics R package (https://github.com/OHDSI/CohortDiagnostics) was run to assess the use of different codes across the databases contributing to the study and identify any codes potentially omitted in error. This allows for considering the validity of the study cohort of patients with the selected cancers and co-morbidities in each database and informs decisions around whether multiple definitions are required.

The study code was based on three R packages currently developed to (1) estimate the prevalence of polypharmacy and co-morbidities (IncidencePrevalence), (2) characterise demographic and clinical characteristics (PatientProfiles), (3) estimate one-year hospitalisation rate and mortality risk (CohortSuvival). These packages included numerous automated unit tests to ensure the validity of the codes, alongside software peer review and user testing. The R package is publicly available via GitHub.

12. RESULTS

All results are available in a web application ("Shiny app") at https://data-dev.darwin-eu.org/P2-C1-009-FrailtyPolypharmacyCancer/. This report includes the main results for all selected cancers of interest combined, and stratified by period, sex, and age categories. In terms of individual cancer types, this report only includes an overall description of these results, and all stratified analyses are available in the Shiny app.

12.1 Participants

The number of individuals contributing to each study objective by database is described in **Table 9**. Overall, there were 464,092 individuals with a diagnosis of the selected cancer types between 2017 and 2022 in the participating databases (IQVIA DA Germany: 226,970; SIDIAP: 140,536; IPCI: 27,480; EBB: 4,485; IQVIA LPD Belgium: 4,748; CPRD GOLD: 59,873). From these, a total of 350,203 had no prior history of cancer (any, excluding non-melanoma skin cancer) and were at least 18 years of age at the time of cancer (Cohort 1) (IQVIA DA Germany: 158,109; SIDIAP: 107,010; IPCI: 24,389; EBB: 3,310; IQVIA LPD Belgium: 2,964; CPRD

GOLD: 54,421). This was the final cohort used to inform objectives 1 and 2. Of these, 231,860 were older adults aged 65 and above. To assess the sub-objective of one-year hospitalisation rate and mortality risk following cancer diagnosis, individuals were required to have one year of potential follow-up following cancer diagnosis, leaving a total of 158,955 individuals aged 18 and above, to assess this outcome (Cohort 2).

Table 9. Study attrition of individuals included in each cohort per database.

	IQVIA DA Germany	SIDIAP	IPCI	EBB	IQVIA LPD Belgium	CPRD GOLD
Database population	43,058,800	8,553,400	2,817,400	211,800	1,119,600	17,412,100
First occurrence of cancer diagnosis (selected cancer types) identified in the database between 01/01/2017 and 31/12/2022, and with 365 days of prior observation	226,970	140,536	2,7480	4,485	4,748	59,873
No prior cancer diagnosis (any, excluding non-melanoma skin cancer) before the diagnosis of selected cancers	158,869	107,348	24,479	3,311	3,016	54,665
At least 18 years of age (Cohort 1)	158,109	107,010	24,389	3,310	2,964	54,421
Minimum of one year of potential follow-up time (Cohort 2)	NA	88,723	20,755	2,769	NA	46,708

Cohort 2 was not created for IQVIA DA Germany and IQVIA LPD Belgium since mortality and hospitalisation information was not available in these databases.

12.2 Demographic Characteristics

Table 10 describes the demographic characteristics of all individuals identified with the selected cancer types in each database. In all databases, the median age ranged between 65 (EBB) and 69 years (IPCI, CPRD GOLD, IQVIA DA Germany, IQVIA LPD Belgium). By age category, most individuals included in the study were 65 years or older at the time of cancer diagnosis (all age groups >= 65 years combined), ranging from 52% in EBB to 64.5% in CPRD GOLD. The defined age groups with the highest proportion of individuals were 45-64 (ranging from 30.5% in IQVIA LPD Belgium to 40% in EBB) and 65-74 (ranging from 26% in SIDIAP to 32.8% in IPCI).

Overall, the distribution of cancer cases by sex was generally similar across all databases, with a slightly higher proportion of women with incident-selected cancers among IPCI, CPRD GOLD, EBB, and IQVIA LPD Belgium. The proportion of each cancer type by each database is available in **Appendix II. Table 1**.

Table 10. Demographic characteristics of all individuals with selected cancer types.

Variable	IPCI N=24,389	CPRD GOLD N=54,421	SIDIAP N=106,991	EBB N=3,310	IQVIA DA Germany N=158,109	IQVIA LPD Belgium N=2,964
Median Age	69	69	68	65	69	69
Age Group: 18 to 44	1142 (4.7%)	2381 (4.4%)	7313 (6.8%)	264 (8%)	8540 (5.4%)	251 (8.5%)
Age Group: 45 to 64	7949 (32.6%)	16945 (31.1%)	37124 (34.7%)	1323 (40%)	51924 (32.8%)	904 (30.5%)
Age Group: 65 to 74	7992 (32.8%)	17256 (31.7%)	27862 (26%)	1020 (30.8%)	43472 (27.5%)	829 (28%)
Age Group: 75 to 84	5545 (22.7%)	13099 (24.1%)	22897 (21.4%)	573 (17.3%)	42937 (27.2%)	682 (23%)
Age Group: 85 to 120	1759 (7.2%)	4740 (8.7%)	11795 (11%)	130 (3.9%)	11236 (7.1%)	298 (10.1%)
Sex: Female	12810 (52.5%)	28532 (52.4%)	53191 (49.7%)	1735 (52.4%)	79995 (50.6%)	1550 (52.3%)
Sex: Male	11579 (47.5%)	25889 (47.6%)	53819 (50.3%)	1575 (47.6%)	78014 (49.3%)	1414 (47.7%)
Sex: Unknown	0 (0%)	0 (0%)	0 (0%)	0 (0%)	100 (0.1%)	0 (0%)

All values are N (%) unless otherwise stated. NA=Counts <5. Selected cancer types: lung, breast, ovary, endometrium, prostate, pancreas, colorectal cancer, lymphoma, leukaemia and myeloma.

12.3 Main Results

12.3.1 Prevalence of Frailty and Polypharmacy

Overall, across all cancer types included in this study, the median frailty score at incident diagnosis of selected cancers ranged between 0.056 (IPCI & IQVIA DA Germany) and 0.139 (EBB) (

Table 11).

Regarding frailty categories, most individuals included in the study were considered fit. The proportion of individuals considered fit varied across databases, highest in IQVIA DA Germany (76.3%) and lowest in EBB (41.7%). Conversely, the prevalence of frailty (including all individuals with mild to severe frailty) ranged between 23.7% (IQVIA DA Germany) and 58.3% (EBB). Across all databases, the proportion of individuals decreased with increasing frailty severity. The prevalence of severe frailty was low, ranging between 0.2% (IQVIA LPD Belgium) and 5% (EBB).

The prevalence of polypharmacy using the >=5 threshold of prescribed medicines ranged between 19% (IQVIA DA Germany) and 56.2% (SIDIAP). The prevalence of polypharmacy decreased in all databases when the threshold increased to >=10 drugs, ranging from 4.3% (IQVIA DA Germany) to 22.9% in SIDIAP.

Table 11. Overall Prevalence of Frailty and Polypharmacy among individuals with selected cancer types.

Variable	IPCI N=24,389	CPRD GOLD N=54,421	SIDIAP N=106,991	EBB N=3,310	IQVIA DA Germany N=158,109	IQVIA LPD Belgium N=2,964
Median frailty score	0.056	0.083	0.111	0.139	0.056	0.083
Frailty category: Fit	18354 (75.3%)	37757 (69.4%)	58943 (55.1%)	1380 (41.7%)	120616 (76.3%)	2219 (74.9%)
Frailty Category: Mild	4886 (20%)	12830 (23.6%)	31054 (29%)	1222 (36.9%)	26266 (16.6%)	673 (22.7%)
Frailty category: Moderate	1028 (4.2%)	3211 (5.9%)	12410 (11.6%)	543 (16.4%)	8626 (5.5%)	67 (2.3%)
Frailty category: Severe	121 (0.5%)	623 (1.1%)	4603 (4.3%)	165 (5%)	2601 (1.6%)	5 (0.2%)
Median number of medications	4	5	5	3	1	4
Polypharmacy >=5	10645 (43.6%)	29905 (55%)	60150 (56.2%)	1263 (38.2%)	29985 (19%)	1288 (43.5%)
Polypharmacy >=10	3552 (14.6%)	11954 (22%)	24454 (22.9%)	183 (5.5%)	6871 (4.3%)	327 (11%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

12.3.2 Prevalence of Conditions Included in the Frailty Score

Some of the conditions included in the frailty score (without counting polypharmacy) returned zero counts. CPRD GOLD had record counts for all conditions, followed by SIDIAP (only 1 condition with zero counts),

while IPCI and IQVIA LPD Belgium were the databases with the highest number (6) of conditions with zero counts. **Table 13** shows the prevalence of conditions included in the frailty score (without polypharmacy) by database. The distribution of conditions varied by database, and some conditions showed marked differences in their prevalence across databases, such as fragility fracture, heart failure, and arthritis, among others. Among conditions reflecting disease state, foot problems returned zero counts in all databases, except CPRD GOLD. Among conditions reflecting symptoms and signs captured, falls also returned zero counts, except for CPRD GOLD, SIDIAP and IQVIA LPD Belgium. Among conditions in the disability domain, housebound and requirement for care returned zero counts in more than one database (IPCI, EBB, IQVIA DA Germany, and IQVIA LPD Belgium for the former; and IPCI, EBB, and IQVIA LPD Belgium for the latter).

The 5 most prevalent conditions in each database were, in IPCI, chronic kidney disease (30.1%), hypertension (28.0%), urinary system disease (17.2%), visual impairment (15.7%), and respiratory disease (14.9%). For CPRD GOLD, chronic kidney disease (30.8%), hypertension (26.9%), Dyspnoea (21.7%), respiratory disease (21.3%), and dizziness (13.4%). For SIDIAP, chronic kidney disease (45.8%), hypertension (44.3%), visual impairment (32.7%), urinary system disease (27.0%), and anaemia (24.0%). For EBB, chronic kidney disease (56.7%), hypertension (53.5%), respiratory disease (43.6%), arthritis (37.1%), and visual impairment (36.4%). For IQVIA DA Germany, hypertension (40.5%), chronic kidney disease (32.3%), respiratory disease (21.7%), thyroid disease (18.5%), and diabetes (14.2%). For IQVIA LPD Belgium, hypertension (50.8%), respiratory disease (33.6%), sleep disturbance (31.2%), chronic kidney disease (23.5%), and diabetes (15.6%).

Table 12. Prevalence of conditions included in the frailty score among all patients with selected cancer types.

Variable	IPCI N=24,389	CPRD GOLD N=54,421	SIDIAP N=106,991	EBB N=3,310	IQVIA DA Germany N=158,109	IQVIA LPD Belgium N=2,964
Disease State						
Anaemia	2264 (9.3%)	5200 (9.6%)	25684 (24%)	745 (22.5%)	15210 (9.6%)	219 (7.4%)
Arthritis	1777 (7.3%)	6207 (11.4%)	12349 (11.5%)	1229 (37.1%)	15352 (9.7%)	515 (17.4%)
Atrial fibrillation	1509 (6.2%)	3848 (7.1%)	9687 (9.1%)	0 (0%)	6128 (3.9%)	0 (0%)
Chronic kidney disease	7349 (30.1%)	16743 (30.8%)	48972 (45.8%)	1878 (56.7%)	51013 (32.3%)	697 (23.5%)
Cerebrovascular disease	1587 (6.5%)	3058 (5.6%)	5406 (5.1%)	453 (13.7%)	12047 (7.6%)	188 (6.3%)
Diabetes	3010 (12.3%)	6746 (12.4%)	21857 (20.4%)	553 (16.7%)	22506 (14.2%)	461 (15.6%)
Foot problems	0 (0%)	3575 (6.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	1511 (6.2%)	5915 (10.9%)	13440 (12.6%)	731 (22.1%)	10670 (6.7%)	134 (4.5%)
Heart failure	894 (3.7%)	1466 (2.7%)	8514 (8%)	1043 (31.5%)	11864 (7.5%)	173 (5.8%)
Heart valve disease	557 (2.3%)	1575 (2.9%)	7663 (7.2%)	159 (4.8%)	8786 (5.6%)	50 (1.7%)
Hypertension	6839 (28%)	14662 (26.9%)	47411 (44.3%)	1772 (53.5%)	63957 (40.5%)	1507 (50.8%)
Hypotension	1747 (7.2%)	2215 (4.1%)	2648 (2.5%)	60 (1.8%)	3660 (2.3%)	68 (2.3%)
Ischaemic heart disease	2148 (8.8%)	4457 (8.2%)	8353 (7.8%)	1003 (30.3%)	20381 (12.9%)	247 (8.3%)
Osteoporosis	807 (3.3%)	2328 (4.3%)	8655 (8.1%)	259 (7.8%)	10566 (6.7%)	353 (11.9%)
Parkinsonism & tremor	144 (0.6%)	1709 (3.1%)	4388 (4.1%)	185 (5.6%)	5902 (3.7%)	132 (4.5%)
Peptic ulcer	199 (0.8%)	857 (1.6%)	2555 (2.4%)	624 (18.9%)	3567 (2.3%)	75 (2.5%)
Peripheral vascular disease	861 (3.5%)	1142 (2.1%)	5098 (4.8%)	245 (7.4%)	9436 (6%)	55 (1.9%)
Respiratory disease	3623 (14.9%)	11610 (21.3%)	20076 (18.8%)	1443 (43.6%)	34348 (21.7%)	997 (33.6%)
Skin ulcer	623 (2.6%)	535 (1%)	3020 (2.8%)	89 (2.7%)	2562 (1.6%)	13 (0.4%)
Thyroid disease	1183 (4.9%)	3932 (7.2%)	13620 (12.7%)	740 (22.4%)	29242 (18.5%)	377 (12.7%)
Urinary system disease	4204 (17.2%)	6536 (12%)	28903 (27%)	837 (25.3%)	21324 (13.5%)	237 (8%)
Symptoms/signs						
Dyspnoea	2649 (10.9%)	11833 (21.7%)	8987 (8.4%)	35 (1.1%)	8182 (5.2%)	11 (0.4%)
Dizziness	2308 (9.5%)	7287 (13.4%)	17898 (16.7%)	409 (12.4%)	13774 (8.7%)	163 (5.5%)

Variable	IPCI N=24,389	CPRD GOLD N=54,421	SIDIAP N=106,991	EBB N=3,310	IQVIA DA Germany N=158,109	IQVIA LPD Belgium N=2,964
Falls	0 (0%)	4668 (8.6%)	5381 (5%)	0 (0%)	0 (0%)	14 (0.5%)
Memory & Cognitive problems	1181 (4.8%)	2346 (4.3%)	9036 (8.4%)	103 (3.1%)	5489 (3.5%)	73 (2.5%)
Sleep disturbance	2828 (11.6%)	5993 (11%)	19260 (18%)	1122 (33.9%)	16664 (10.5%)	926 (31.2%)
Urinary incontinence	3085 (12.6%)	5972 (11%)	13605 (12.7%)	227 (6.9%)	10678 (6.8%)	152 (5.1%)
Weight loss & anorexia	1849 (7.6%)	2776 (5.1%)	5867 (5.5%)	32 (1%)	5030 (3.2%)	19 (0.6%)
Disability						
Activity limitation	0 (0%)	60 (0.1%)	3759 (3.5%)	NA (NA%)	NA (NA%)	0 (0%)
Hearing impairment	1487 (6.1%)	5473 (10.1%)	13152 (12.3%)	657 (19.8%)	8779 (5.6%)	16 (0.5%)
Housebound	0 (0%)	782 (1.4%)	4374 (4.1%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	987 (1.8%)	966 (0.9%)	NA (NA%)	1167 (0.7%)	0 (0%)
Requiring care	0 (0%)	910 (1.7%)	4278 (4%)	0 (0%)	946 (0.6%)	0 (0%)
Social vulnerability	1494 (6.1%)	680 (1.2%)	8781 (8.2%)	12 (0.4%)	250 (0.2%)	24 (0.8%)
Visual impairment	3826 (15.7%)	6290 (11.6%)	34942 (32.7%)	1206 (36.4%)	12551 (7.9%)	164 (5.5%)

All values are N (%) unless otherwise stated. NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

12.3.3 Prevalence Frailty and Polypharmacy by Period (pre- and post-2020)

Table 13 displays the characteristics of the overall cancer patients, prevalence of frailty, and polypharmacy by period (pre- and post-2020) and database.

Regarding age, EBB's median age increased from 64 to 66 in the post-2020 period, while the other databases varied slightly. The median frailty score remained unchanged in all databases, except for IPCI and EBB, which increased in the post-2020 period. However, there was a small increase in the proportion of patients within the mild, moderate, and severe frailty categories during the post-2020 period in all databases, except for CPRD GOLD and IQVIA DA Germany, which remained mostly unchanged. The prevalence of polypharmacy varied slightly.

The prevalence of the conditions in the frailty score varied slightly between periods. Some conditions displayed an increase by at least 5% in their prevalence in the post-2020 period and in at least one database: chronic kidney disease (5.5% in IQVIA LPD Belgium and 6.0% in SIDIAP) and fragility fracture (7.3% in EBB).

Table 13. Demographic characteristics and prevalence of frailty and polypharmacy by period (pre- and post-2020).

Variable	IPCI		CPRD GOLD		SIDIAP	EBB	IQVIA DA Germany			IQVIA LPD Belgium		
Period	Pre-2020 N=12,560	Post-2020 N=11,829	Pre-2020 N=30,627	Post-2020 N=23,794	Pre-2020 N=55,271	Post-2020 N=51,739	Pre-2020 N=1,685	Post-2020 N=1,625	Pre-2020 N=77,110	Post-2020 N=80,899	Pre-2020 N=1,664	Post-2020 N=1,300
Median Age (years)	69	69	69	70	68	68	64	66	69	69	68	69
Age Group: 18 to 44	564 (4.5%)	578 (4.9%)	1263 (4.1%)	1118 (4.7%)	3930 (7.1%)	3383 (6.5%)	143 (8.5%)	121 (7.4%)	4110 (5.3%)	4430 (5.5%)	133 (8%)	118 (9.1%)
Age Group: 45 to 64	4224 (33.6%)	3725 (31.5%)	9742 (31.8%)	7203 (30.3%)	19280 (34.9%)	17844 (34.5%)	706 (41.9%)	617 (38%)	25584 (33.2%)	26340 (32.5%)	521 (31.3%)	383 (29.5%)
Age Group: 65 to 74	4154 (33.1%)	3838 (32.4%)	9794 (32%)	7462 (31.4%)	14425 (26.1%)	13437 (26%)	505 (30%)	515 (31.7%)	20734 (26.9%)	22738 (28.1%)	480 (28.8%)	349 (26.8%)
Age Group: 75 to 84	2745 (21.9%)	2800 (23.7%)	7175 (23.4%)	5924 (24.9%)	11678 (21.1%)	11219 (21.7%)	272 (16.1%)	301 (18.5%)	21864 (28.3%)	21073 (26%)	388 (23.3%)	294 (22.6%)
Age Group: 85 to 120	871 (6.9%)	888 (7.5%)	2653 (8.7%)	2087 (8.8%)	5949 (10.8%)	5846 (11.3%)	59 (3.5%)	71 (4.4%)	4874 (6.3%)	6362 (7.9%)	142 (8.5%)	156 (12%)
Sex: Female	6547 (52.1%)	6263 (52.9%)	16104 (52.6%)	12428 (52.2%)	26584 (48.1%)	26607 (51.4%)	928 (55.1%)	807 (49.7%)	39017 (50.6%)	40978 (50.6%)	901 (54.1%)	649 (49.9%)
Sex: Male	6013 (47.9%)	5566 (47.1%)	14523 (47.4%)	11366 (47.8%)	28687 (51.9%)	25132 (48.6%)	757 (44.9%)	818 (50.3%)	38093 (49.4%)	39921 (49.3%)	763 (45.9%)	651 (50.1%)
Median frailty score	0.056	0.083	0.083	0.083	0.111	0.111	0.139	0.167	0.056	0.056	0.083	0.083
Frailty category: Fit	9747 (77.6%)	8607 (72.8%)	21277 (69.5%)	16480 (69.3%)	31988 (57.9%)	26955 (52.1%)	747 (44.3%)	633 (39%)	59086 (76.6%)	61530 (76%)	1294 (77.8%)	925 (71.2%)
Frailty Category: Mild	2334 (18.6%)	2552 (21.6%)	7184 (23.5%)	5646 (23.7%)	15638 (28.3%)	15416 (29.8%)	599 (35.5%)	623 (38.3%)	12786 (16.6%)	13480 (16.7%)	343 (20.6%)	330 (25.4%)

Variable	IPCI		CPRD GOLD		SIDIAP	EBB	IQVIA DA Germany			IQVIA LPD Belgium		
Period	Pre-2020 N=12,560	Post-2020 N=11,829	Pre-2020 N=30,627	Post-2020 N=23,794	Pre-2020 N=55,271	Post-2020 N=51,739	Pre-2020 N=1,685	Post-2020 N=1,625	Pre-2020 N=77,110	Post-2020 N=80,899	Pre-2020 N=1,664	Post-2020 N=1,300
Frailty category: Moderate	435 (3.5%)	593 (5%)	1808 (5.9%)	1403 (5.9%)	5765 (10.4%)	6645 (12.8%)	260 (15.4%)	283 (17.4%)	4070 (5.3%)	4556 (5.6%)	26 (1.6%)	41 (3.2%)
Frailty category: Severe	44 (0.4%)	77 (0.7%)	358 (1.2%)	265 (1.1%)	1880 (3.4%)	2723 (5.3%)	79 (4.7%)	86 (5.3%)	1224 (1.6%)	1377 (1.7%)	NA (NA%)	NA (NA%)
Median number of medications	4	4	5	5	5	5	3	4	1	1	4	4
Polypharmacy >=5	5454 (43.4%)	5191 (43.9%)	16616 (54.3%)	13289 (55.9%)	30753 (55.6%)	29397 (56.8%)	642 (38.1%)	621 (38.2%)	14816 (19.2%)	15169 (18.7%)	703 (42.2%)	585 (45%)
Polypharmacy >=10	1798 (14.3%)	1754 (14.8%)	6470 (21.1%)	5484 (23%)	12095 (21.9%)	12359 (23.9%)	97 (5.8%)	86 (5.3%)	3385 (4.4%)	3486 (4.3%)	173 (10.4%)	154 (11.8%)
Disease State												
Arthritis	840 (6.7%)	937 (7.9%)	3547 (11.6%)	2660 (11.2%)	5685 (10.3%)	6664 (12.9%)	611 (36.3%)	618 (38%)	7149 (9.3%)	8203 (10.1%)	245 (14.7%)	270 (20.8%)
Atrial fibrillation	743 (5.9%)	766 (6.5%)	2063 (6.7%)	1785 (7.5%)	4967 (9%)	4720 (9.1%)	0 (0%)	0 (0%)	2889 (3.7%)	3239 (4%)	0 (0%)	0 (0%)
Chronic kidney disease	3507 (27.9%)	3842 (32.5%)	9567 (31.2%)	7176 (30.2%)	23690 (42.9%)	25282 (48.9%)	921 (54.7%)	957 (58.9%)	24575 (31.8%)	26438 (32.7%)	351 (21.1%)	346 (26.6%)
Cerebrovascular disease	771 (6.1%)	816 (6.9%)	1590 (5.2%)	1468 (6.2%)	2656 (4.8%)	2750 (5.3%)	230 (13.6%)	223 (13.7%)	5818 (7.5%)	6229 (7.7%)	98 (5.9%)	90 (6.9%)
Diabetes	1517 (12.1%)	1493 (12.6%)	3654 (11.9%)	3092 (13%)	11181 (20.2%)	10676 (20.6%)	293 (17.4%)	260 (16%)	11063 (14.3%)	11443 (14.1%)	237 (14.2%)	224 (17.2%)

Variable	IPCI		CPRD GOLD		SIDIAP	EBB	IQVIA DA Germany			IQVIA LPD Belgium		
Period	Pre-2020 N=12,560	Post-2020 N=11,829	Pre-2020 N=30,627	Post-2020 N=23,794	Pre-2020 N=55,271	Post-2020 N=51,739	Pre-2020 N=1,685	Post-2020 N=1,625	Pre-2020 N=77,110	Post-2020 N=80,899	Pre-2020 N=1,664	Post-2020 N=1,300
Foot problems	0 (0%)	0 (0%)	2060 (6.7%)	1515 (6.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	673 (5.4%)	838 (7.1%)	3153 (10.3%)	2762 (11.6%)	6520 (11.8%)	6920 (13.4%)	312 (18.5%)	419 (25.8%)	4993 (6.5%)	5677 (7%)	76 (4.6%)	58 (4.5%)
Heart failure	462 (3.7%)	432 (3.7%)	794 (2.6%)	672 (2.8%)	4301 (7.8%)	4213 (8.1%)	542 (32.2%)	501 (30.8%)	5784 (7.5%)	6080 (7.5%)	84 (5%)	89 (6.8%)
Heart valve disease	289 (2.3%)	268 (2.3%)	840 (2.7%)	735 (3.1%)	3718 (6.7%)	3945 (7.6%)	76 (4.5%)	83 (5.1%)	4200 (5.4%)	4586 (5.7%)	29 (1.7%)	21 (1.6%)
Hypertension	3509 (27.9%)	3330 (28.2%)	8372 (27.3%)	6290 (26.4%)	24148 (43.7%)	23263 (45%)	893 (53%)	879 (54.1%)	31429 (40.7%)	32528 (40.2%)	824 (49.5%)	683 (52.5%)
Hypotension	835 (6.6%)	912 (7.7%)	1277 (4.2%)	938 (3.9%)	1159 (2.1%)	1489 (2.9%)	23 (1.4%)	37 (2.3%)	1758 (2.3%)	1902 (2.3%)	37 (2.2%)	31 (2.4%)
Ischaemic heart disease	1041 (8.3%)	1107 (9.4%)	2544 (8.3%)	1913 (8%)	4248 (7.7%)	4105 (7.9%)	514 (30.5%)	489 (30.1%)	10330 (13.4%)	10051 (12.4%)	135 (8.1%)	112 (8.6%)
Osteoporosis	406 (3.2%)	401 (3.4%)	1314 (4.3%)	1014 (4.3%)	4329 (7.8%)	4326 (8.4%)	132 (7.8%)	127 (7.8%)	5306 (6.9%)	5260 (6.5%)	198 (11.9%)	155 (11.9%)
Parkinsonism & tremor	76 (0.6%)	68 (0.6%)	960 (3.1%)	749 (3.1%)	2163 (3.9%)	2225 (4.3%)	73 (4.3%)	112 (6.9%)	2789 (3.6%)	3113 (3.8%)	65 (3.9%)	67 (5.2%)
Peptic ulcer	96 (0.8%)	103 (0.9%)	486 (1.6%)	371 (1.6%)	1296 (2.3%)	1259 (2.4%)	310 (18.4%)	314 (19.3%)	1757 (2.3%)	1810 (2.2%)	37 (2.2%)	38 (2.9%)
Peripheral vascular disease	415 (3.3%)	446 (3.8%)	645 (2.1%)	497 (2.1%)	2590 (4.7%)	2508 (4.8%)	123 (7.3%)	122 (7.5%)	4731 (6.1%)	4705 (5.8%)	30 (1.8%)	25 (1.9%)
Respiratory disease	1863 (14.8%)	1760 (14.9%)	6560 (21.4%)	5050 (21.2%)	10207 (18.5%)	9869 (19.1%)	699 (41.5%)	744 (45.8%)	16676 (21.6%)	17672 (21.8%)	543 (32.6%)	454 (34.9%)
Skin ulcer	294 (2.3%)	329 (2.8%)	312 (1%)	223 (0.9%)	1492 (2.7%)	1528 (3%)	44 (2.6%)	45 (2.8%)	1203 (1.6%)	1359 (1.7%)	6 (0.4%)	7 (0.5%)

Variable	IPCI		CPRD GOLD		SIDIAP	EBB	IQVIA DA Germany			IQVIA LPD Belgium		
Period	Pre-2020 N=12,560	Post-2020 N=11,829	Pre-2020 N=30,627	Post-2020 N=23,794	Pre-2020 N=55,271	Post-2020 N=51,739	Pre-2020 N=1,685	Post-2020 N=1,625	Pre-2020 N=77,110	Post-2020 N=80,899	Pre-2020 N=1,664	Post-2020 N=1,300
Thyroid disease	562 (4.5%)	621 (5.2%)	2291 (7.5%)	1641 (6.9%)	6395 (11.6%)	7225 (14%)	394 (23.4%)	346 (21.3%)	14228 (18.4%)	15014 (18.5%)	210 (12.6%)	167 (12.8%)
Urinary system disease	1994 (15.9%)	2210 (18.7%)	3700 (12.1%)	2836 (11.9%)	13013 (23.5%)	15890 (30.7%)	411 (24.4%)	426 (26.2%)	10008 (13%)	11316 (14%)	110 (6.6%)	127 (9.8%)
Symptoms/signs												
Dyspnoea	1240 (9.9%)	1409 (11.9%)	6843 (22.3%)	4990 (21%)	3990 (7.2%)	4997 (9.7%)	12 (0.7%)	23 (1.4%)	3704 (4.8%)	4478 (5.5%)	7 (0.4%)	NA (NA%)
Dizziness	1077 (8.6%)	1231 (10.4%)	4184 (13.7%)	3103 (13%)	8157 (14.8%)	9741 (18.8%)	192 (11.4%)	217 (13.4%)	6521 (8.5%)	7253 (9%)	81 (4.9%)	82 (6.3%)
Falls	0 (0%)	0 (0%)	2728 (8.9%)	1940 (8.2%)	2438 (4.4%)	2943 (5.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6 (0.4%)	8 (0.6%)
Memory & Cognitive problems	558 (4.4%)	623 (5.3%)	1361 (4.4%)	985 (4.1%)	4441 (8%)	4595 (8.9%)	43 (2.6%)	60 (3.7%)	2683 (3.5%)	2806 (3.5%)	40 (2.4%)	33 (2.5%)
Sleep disturbance	1346 (10.7%)	1482 (12.5%)	3397 (11.1%)	2596 (10.9%)	9006 (16.3%)	10254 (19.8%)	550 (32.6%)	572 (35.2%)	7779 (10.1%)	8885 (11%)	492 (29.6%)	434 (33.4%)
Urinary incontinence	1429 (11.4%)	1656 (14%)	3521 (11.5%)	2451 (10.3%)	6575 (11.9%)	7030 (13.6%)	108 (6.4%)	119 (7.3%)	5279 (6.8%)	5399 (6.7%)	75 (4.5%)	77 (5.9%)
Weight loss & anorexia	848 (6.8%)	1001 (8.5%)	1570 (5.1%)	1206 (5.1%)	2515 (4.6%)	3352 (6.5%)	11 (0.7%)	21 (1.3%)	2262 (2.9%)	2768 (3.4%)	9 (0.5%)	10 (0.8%)
Disability												
Activity limitation	0 (0%)	0 (0%)	32 (0.1%)	28 (0.1%)	1646 (3%)	2113 (4.1%)	NA (NA%)	0 (0%)	NA (NA%)	NA (NA%)	0 (0%)	0 (0%)

Variable	IPCI		CPRD GOLD		SIDIAP	EBB	IQVIA DA Germany			IQVIA LPD Belgium		
Period	Pre-2020 N=12,560	Post-2020 N=11,829	Pre-2020 N=30,627	Post-2020 N=23,794	Pre-2020 N=55,271	Post-2020 N=51,739	Pre-2020 N=1,685	Post-2020 N=1,625	Pre-2020 N=77,110	Post-2020 N=80,899	Pre-2020 N=1,664	Post-2020 N=1,300
Hearing impairment	706 (5.6%)	781 (6.6%)	3124 (10.2%)	2349 (9.9%)	6410 (11.6%)	6742 (13%)	317 (18.8%)	340 (20.9%)	4336 (5.6%)	4443 (5.5%)	11 (0.7%)	5 (0.4%)
Housebound	0 (0%)	0 (0%)	334 (1.1%)	448 (1.9%)	2139 (3.9%)	2235 (4.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	0 (0%)	550 (1.8%)	437 (1.8%)	369 (0.7%)	597 (1.2%)	0 (0%)	NA (NA%)	433 (0.6%)	734 (0.9%)	0 (0%)	0 (0%)
Requiring care	0 (0%)	0 (0%)	493 (1.6%)	417 (1.8%)	1656 (3%)	2622 (5.1%)	0 (0%)	0 (0%)	419 (0.5%)	527 (0.7%)	0 (0%)	0 (0%)
Social vulnerability	617 (4.9%)	877 (7.4%)	365 (1.2%)	315 (1.3%)	4121 (7.5%)	4660 (9%)	NA (NA%)	9 (0.6%)	101 (0.1%)	149 (0.2%)	8 (0.5%)	16 (1.2%)
Visual impairment	1799 (14.3%)	2027 (17.1%)	3548 (11.6%)	2742 (11.5%)	17167 (31.1%)	17775 (34.4%)	578 (34.3%)	628 (38.6%)	6197 (8%)	6354 (7.8%)	80 (4.8%)	84 (6.5%)
Abnormal laboratory value												
Anaemia	1131 (9%)	1133 (9.6%)	2907 (9.5%)	2293 (9.6%)	12835 (23.2%)	12849 (24.8%)	348 (20.7%)	397 (24.4%)	7171 (9.3%)	8039 (9.9%)	113 (6.8%)	106 (8.2%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Counts<5.

12.3.4 Characteristics of Individuals according to Frailty Category

The characteristics of individuals by frailty category are summarised in **Tables 15-18**.
Table 14 describes the characteristics of fit individuals, while **Table 15** describes mild frailty, **Table 16** moderate frailty, and **Table 17** severe frailty.

Overall, there was no clear sex predominance among individuals considered fit. Mild frailty displayed some variation in sex predominance by database, while for moderate and severe frailty, there was a clear predominance of female sex in all databases, which increased in proportion with increasing frailty severity.

The proportion of older individuals increased with increasing frailty score. The mean age among those individuals in the fit and severe frailty categories varied from 55 to 66 and from 75 to 90 years, respectively.

Regarding polypharmacy (using the =>5 drugs threshold), among fit, the prevalence of polypharmacy was inconsistent among databases and ranged between 6.6% (IQVIA DA Germany) and 39.8% (CPRD GOLD). Among frail, the prevalence of polypharmacy increased as frailty severity increased, and in severe frailty, polypharmacy was 89% and above. The prevalence of polypharmacy varied across databases. For example, mild frailty had a prevalence of polypharmacy between 45.7% in EBB and 86.9% in CPRD GOLD. However, for moderate frailty, the prevalence of polypharmacy was above 72% in all databases, and for severe frailty, it was consistently above 89%.

Regarding the conditions included in the frailty score, the prevalence increased with increasing frailty severity category. Within the severe frailty category (**Table 17**), some conditions reached a prevalence above 45% in all databases, such as chronic kidney disease (ranging between 90.1% in IPCI and 95.8% in EBB), hypertension (63.2% in CPRD GOLD to 96.3% in IQVIA DA Germany), and sleep disturbance (49% in SIDIAP to 85.5% in EBB) (Results on severe frailty in IQVIA LPD Belgium are not described because of low counts).

Table 14. Characteristics of Individuals with selected cancers within the fit frailty category, by databases.

Variable	IPCI N=18,354	CPRD GOLD N=37,757	SIDIAP N=58,943	EBB N=1,380	IQVIA DA Germany N=120,542	IQVIA LPD Belgium N=2,219
Median Age	66	66	61	59	67	66
Age Group: 18 to 44	1103 (6%)	2255 (6%)	6720 (11.4%)	192 (13.9%)	7872 (6.5%)	236 (10.6%)
Age Group: 45 to 64	7116 (38.8%)	14464 (38.3%)	28800 (48.9%)	765 (55.4%)	44080 (36.5%)	767 (34.6%)
Age Group: 65 to 74	6187 (33.7%)	12321 (32.6%)	15075 (25.6%)	314 (22.8%)	33447 (27.7%)	614 (27.7%)
Age Group: 75 to 84	3220 (17.5%)	6943 (18.4%)	6732 (11.4%)	99 (7.2%)	29345 (24.3%)	423 (19.1%)
Age Group: 85 to 120	726 (4%)	1774 (4.7%)	1598 (2.7%)	10 (0.7%)	5872 (4.9%)	179 (8.1%)
Sex: Female	9465 (51.6%)	19699 (52.2%)	29437 (49.9%)	675 (48.9%)	61360 (50.9%)	1155 (52.1%)
Sex: Male	8889 (48.4%)	18058 (47.8%)	29506 (50.1%)	705 (51.1%)	59182 (49.1%)	1064 (47.9%)
Median frailty score	0.056	0.056	0.056	0.083	0.028	0.056
Median number of medications	3	4	3	2	0	3
Polypharmacy >=5	5822 (31.7%)	15040 (39.8%)	17446 (29.6%)	161 (11.7%)	7954 (6.6%)	682 (30.7%)
Polypharmacy >=10	1527 (8.3%)	4219 (11.2%)	3122 (5.3%)	6 (0.4%)	914 (0.8%)	108 (4.9%)
Disease State						
Arthritis	927 (5.1%)	2680 (7.1%)	4331 (7.3%)	313 (22.7%)	6636 (5.5%)	279 (12.6%)
Atrial fibrillation	468 (2.5%)	978 (2.6%)	976 (1.7%)	0 (0%)	1688 (1.4%)	0 (0%)
Chronic kidney disease	3491 (19%)	6559 (17.4%)	14343 (24.3%)	473 (34.3%)	26488 (22%)	339 (15.3%)
Cerebrovascular disease	544 (3%)	828 (2.2%)	565 (1%)	42 (3%)	3544 (2.9%)	78 (3.5%)
Diabetes	1190 (6.5%)	2377 (6.3%)	4683 (7.9%)	58 (4.2%)	8009 (6.6%)	201 (9.1%)
Foot problems	0 (0%)	852 (2.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	686 (3.7%)	2513 (6.7%)	3289 (5.6%)	172 (12.5%)	3704 (3.1%)	54 (2.4%)

Variable	IPCI N=18,354	CPRD GOLD N=37,757	SIDIAP N=58,943	EBB N=1,380	IQVIA DA Germany N=120,542	IQVIA LPD Belgium N=2,219
Heart failure	190 (1%)	173 (0.5%)	380 (0.6%)	82 (5.9%)	2538 (2.1%)	39 (1.8%)
Heart valve disease	166 (0.9%)	344 (0.9%)	808 (1.4%)	18 (1.3%)	3044 (2.5%)	21 (0.9%)
Hypertension	3533 (19.2%)	6935 (18.4%)	14157 (24%)	388 (28.1%)	33218 (27.5%)	873 (39.3%)
Hypotension	724 (3.9%)	545 (1.4%)	416 (0.7%)	11 (0.8%)	1065 (0.9%)	24 (1.1%)
Ischaemic heart disease	809 (4.4%)	1293 (3.4%)	1040 (1.8%)	114 (8.3%)	6516 (5.4%)	87 (3.9%)
Osteoporosis	262 (1.4%)	663 (1.8%)	1596 (2.7%)	12 (0.9%)	4479 (3.7%)	179 (8.1%)
Parkinsonism & tremor	50 (0.3%)	488 (1.3%)	604 (1%)	31 (2.2%)	2030 (1.7%)	53 (2.4%)
Peptic ulcer	81 (0.4%)	266 (0.7%)	637 (1.1%)	115 (8.3%)	945 (0.8%)	39 (1.8%)
Peripheral vascular disease	229 (1.2%)	273 (0.7%)	553 (0.9%)	16 (1.2%)	2133 (1.8%)	19 (0.9%)
Respiratory disease	1649 (9%)	4610 (12.2%)	5309 (9%)	396 (28.7%)	16162 (13.4%)	567 (25.6%)
Skin ulcer	177 (1%)	125 (0.3%)	284 (0.5%)	20 (1.4%)	440 (0.4%)	5 (0.2%)
Thyroid disease	548 (3%)	1603 (4.2%)	4327 (7.3%)	132 (9.6%)	12387 (10.3%)	206 (9.3%)
Urinary system disease	1715 (9.3%)	1837 (4.9%)	7518 (12.8%)	157 (11.4%)	9432 (7.8%)	72 (3.2%)
Symptoms/signs						
Dyspnoea	1082 (5.9%)	3663 (9.7%)	1433 (2.4%)	NA (NA%)	2053 (1.7%)	5 (0.2%)
Dizziness	915 (5%)	2456 (6.5%)	4761 (8.1%)	64 (4.6%)	4088 (3.4%)	54 (2.4%)
Falls	0 (0%)	1160 (3.1%)	627 (1.1%)	0 (0%)	0 (0%)	NA (NA%)
Memory & Cognitive problems	372 (2%)	614 (1.6%)	890 (1.5%)	9 (0.7%)	1234 (1%)	28 (1.3%)
Sleep disturbance	1218 (6.6%)	2087 (5.5%)	4926 (8.4%)	176 (12.8%)	5587 (4.6%)	504 (22.7%)
Urinary incontinence	1374 (7.5%)	1903 (5%)	1510 (2.6%)	34 (2.5%)	4809 (4%)	61 (2.7%)
Weight loss & anorexia	711 (3.9%)	883 (2.3%)	1501 (2.5%)	NA (NA%)	1544 (1.3%)	7 (0.3%)
Disability						

Variable	IPCI N=18,354	CPRD GOLD N=37,757	SIDIAP N=58,943	EBB N=1,380	IQVIA DA Germany N=120,542	IQVIA LPD Belgium N=2,219
Activity limitation	0 (0%)	6 (0%)	531 (0.9%)	0 (0%)	NA (NA%)	0 (0%)
Hearing impairment	619 (3.4%)	2044 (5.4%)	3209 (5.4%)	119 (8.6%)	3925 (3.3%)	NA (NA%)
Housebound	0 (0%)	157 (0.4%)	122 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	130 (0.3%)	53 (0.1%)	0 (0%)	227 (0.2%)	0 (0%)
Requiring care	0 (0%)	256 (0.7%)	202 (0.3%)	0 (0%)	100 (0.1%)	0 (0%)
Social vulnerability	414 (2.3%)	176 (0.5%)	1467 (2.5%)	NA (NA%)	85 (0.1%)	17 (0.8%)
Visual impairment	1683 (9.2%)	2024 (5.4%)	8518 (14.5%)	191 (13.8%)	2942 (2.4%)	58 (2.6%)
Abnormal laboratory value						
Anaemia	886 (4.8%)	1742 (4.6%)	6601 (11.2%)	205 (14.9%)	4800 (4%)	90 (4.1%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Table 15. Characteristics of Individuals with selected cancers within the mild frailty category, by databases.

Variable	IPCI N=4,886	CPRD GOLD N=12,830	SIDIAP N=31,054	EBB N=1,222	IQVIA DA Germany N=26,250	IQVIA LPD Belgium N=673
Median Age	75	75	73	66	73	74
Age Group: 18 to 44	37 (0.8%)	121 (0.9%)	552 (1.8%)	68 (5.6%)	610 (2.3%)	15 (2.2%)
Age Group: 45 to 64	760 (15.6%)	2168 (16.9%)	7098 (22.9%)	456 (37.3%)	6380 (24.3%)	128 (19%)
Age Group: 65 to 74	1561 (31.9%)	4059 (31.6%)	9780 (31.5%)	436 (35.7%)	7454 (28.4%)	199 (29.6%)
Age Group: 75 to 84	1801 (36.9%)	4568 (35.6%)	9559 (30.8%)	218 (17.8%)	8906 (33.9%)	237 (35.2%)
Age Group: 85 to 120	727 (14.9%)	1914 (14.9%)	4064 (13.1%)	44 (3.6%)	2916 (11.1%)	94 (14%)

Variable	IPCI N=4,886	CPRD GOLD N=12,830	SIDIAP N=31,054	EBB N=1,222	IQVIA DA Germany N=26,250	IQVIA LPD Belgium N=673
Sex: Female	2639 (54%)	6561 (51.1%)	14588 (47%)	633 (51.8%)	12532 (47.7%)	347 (51.6%)
Sex: Male	2247 (46%)	6269 (48.9%)	16466 (53%)	589 (48.2%)	13718 (52.2%)	326 (48.4%)
Median frailty score	0.167	0.167	0.167	0.167	0.167	0.167
Median number of medications	7	8	8	4	4	7
Polypharmacy >=5	3799 (77.8%)	11143 (86.9%)	26187 (84.3%)	558 (45.7%)	12985 (49.4%)	539 (80.1%)
Polypharmacy >=10	1465 (30%)	5174 (40.3%)	9983 (32.1%)	49 (4%)	2694 (10.3%)	175 (26%)
Disease State						
Arthritis	610 (12.5%)	2442 (19%)	4826 (15.5%)	538 (44%)	4893 (18.6%)	204 (30.3%)
Atrial fibrillation	690 (14.1%)	1824 (14.2%)	3250 (10.5%)	0 (0%)	2309 (8.8%)	0 (0%)
Chronic kidney disease	2906 (59.5%)	7081 (55.2%)	19942 (64.2%)	793 (64.9%)	15183 (57.8%)	300 (44.6%)
Cerebrovascular disease	710 (14.5%)	1376 (10.7%)	1919 (6.2%)	142 (11.6%)	4539 (17.3%)	92 (13.7%)
Diabetes	1338 (27.4%)	2918 (22.7%)	9165 (29.5%)	230 (18.8%)	8741 (33.3%)	225 (33.4%)
Foot problems	0 (0%)	1590 (12.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	556 (11.4%)	2214 (17.3%)	4638 (14.9%)	300 (24.5%)	3541 (13.5%)	60 (8.9%)
Heart failure	389 (8%)	696 (5.4%)	2142 (6.9%)	422 (34.5%)	4527 (17.2%)	105 (15.6%)
Heart valve disease	251 (5.1%)	716 (5.6%)	2472 (8%)	52 (4.3%)	3181 (12.1%)	20 (3%)
Hypertension	2537 (51.9%)	5626 (43.9%)	19298 (62.1%)	784 (64.2%)	20491 (78%)	566 (84.1%)
Hypotension	695 (14.2%)	895 (7%)	776 (2.5%)	27 (2.2%)	1292 (4.9%)	34 (5.1%)
Ischaemic heart disease	934 (19.1%)	2005 (15.6%)	3176 (10.2%)	407 (33.3%)	7806 (29.7%)	130 (19.3%)
Osteoporosis	355 (7.3%)	1003 (7.8%)	3166 (10.2%)	88 (7.2%)	3079 (11.7%)	142 (21.1%)
Parkinsonism & tremor	62 (1.3%)	691 (5.4%)	1497 (4.8%)	63 (5.2%)	1817 (6.9%)	66 (9.8%)
Peptic ulcer	89 (1.8%)	385 (3%)	930 (3%)	229 (18.7%)	1275 (4.9%)	30 (4.5%)

Variable	IPCI N=4,886	CPRD GOLD N=12,830	SIDIAP N=31,054	EBB N=1,222	IQVIA DA Germany N=26,250	IQVIA LPD Belgium N=673
Peripheral vascular disease	401 (8.2%)	523 (4.1%)	1881 (6.1%)	77 (6.3%)	3819 (14.5%)	27 (4%)
Respiratory disease	1464 (30%)	4909 (38.3%)	8045 (25.9%)	587 (48%)	11237 (42.8%)	378 (56.2%)
Skin ulcer	269 (5.5%)	202 (1.6%)	801 (2.6%)	21 (1.7%)	831 (3.2%)	7 (1%)
Thyroid disease	441 (9%)	1546 (12%)	5106 (16.4%)	307 (25.1%)	10472 (39.9%)	142 (21.1%)
Urinary system disease	1822 (37.3%)	2919 (22.8%)	11433 (36.8%)	355 (29.1%)	6639 (25.3%)	130 (19.3%)
Symptoms/signs						
Dyspnoea	1063 (21.8%)	5467 (42.6%)	3100 (10%)	10 (0.8%)	2973 (11.3%)	6 (0.9%)
Dizziness	962 (19.7%)	3011 (23.5%)	6937 (22.3%)	154 (12.6%)	4898 (18.6%)	93 (13.8%)
Falls	0 (0%)	1943 (15.1%)	1592 (5.1%)	0 (0%)	0 (0%)	10 (1.5%)
Memory & Cognitive problems	513 (10.5%)	996 (7.8%)	2994 (9.6%)	26 (2.1%)	1866 (7.1%)	33 (4.9%)
Sleep disturbance	1121 (22.9%)	2466 (19.2%)	7581 (24.4%)	473 (38.7%)	6196 (23.6%)	366 (54.4%)
Urinary incontinence	1168 (23.9%)	2552 (19.9%)	4418 (14.2%)	73 (6%)	2652 (10.1%)	72 (10.7%)
Weight loss & anorexia	765 (15.7%)	1126 (8.8%)	2178 (7%)	13 (1.1%)	1829 (7%)	8 (1.2%)
Disability						
Activity limitation	0 (0%)	18 (0.1%)	1332 (4.3%)	0 (0%)	0 (0%)	0 (0%)
Hearing impairment	609 (12.5%)	2253 (17.6%)	5137 (16.5%)	251 (20.5%)	2363 (9%)	8 (1.2%)
Housebound	0 (0%)	329 (2.6%)	758 (2.4%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	382 (3%)	211 (0.7%)	0 (0%)	321 (1.2%)	0 (0%)
Requiring care	0 (0%)	353 (2.8%)	912 (2.9%)	0 (0%)	338 (1.3%)	0 (0%)
Social vulnerability	688 (14.1%)	270 (2.1%)	3033 (9.8%)	5 (0.4%)	97 (0.4%)	6 (0.9%)
Visual impairment	1549 (31.7%)	2728 (21.3%)	14611 (47.1%)	493 (40.3%)	4944 (18.8%)	91 (13.5%)
Abnormal laboratory value						

Variable	IPCI N=4,886	CPRD GOLD N=12,830	SIDIAP N=31,054	EBB N=1,222	IQVIA DA Germany N=26,250	IQVIA LPD Belgium N=673
Anaemia	928 (19%)	2109 (16.4%)	9113 (29.3%)	285 (23.3%)	5515 (21%)	106 (15.8%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

Table 16. Characteristics of Individuals with selected cancers within the moderate frailty category, by databases.

Variable	IPCI N=1,028	CPRD GOLD N=3,211	SIDIAP N=12,410	EBB N=543	IQVIA DA Germany N=8,618	IQVIA LPD Belgium N=67
Median Age	79	79	80	74	77	79
Age Group: 18 to 44	NA (NA%)	NA (NA%)	37 (0.3%)	NA (NA%)	58 (0.7%)	0 (0%)
Age Group: 45 to 64	70 (6.8%)	286 (8.9%)	1092 (8.8%)	88 (16.2%)	1264 (14.7%)	9 (13.4%)
Age Group: 65 to 74	228 (22.2%)	753 (23.5%)	2500 (20.1%)	209 (38.5%)	2110 (24.5%)	15 (22.4%)
Age Group: 75 to 84	461 (44.8%)	1337 (41.6%)	4905 (39.5%)	189 (34.8%)	3515 (40.7%)	22 (32.8%)
Age Group: 85 to 120	267 (26%)	831 (25.9%)	3876 (31.2%)	54 (9.9%)	1679 (19.5%)	21 (31.3%)
Sex: Female	626 (60.9%)	1866 (58.1%)	6441 (51.9%)	309 (56.9%)	4567 (52.9%)	44 (65.7%)
Sex: Male	402 (39.1%)	1345 (41.9%)	5969 (48.1%)	234 (43.1%)	4051 (47%)	23 (34.3%)
Median frailty score	0.278	0.278	0.278	0.278	0.278	0.25
Median number of medications	9	11	11	6	7	11
Polypharmacy >=5	915 (89%)	3108 (96.8%)	11979 (96.5%)	395 (72.7%)	6730 (78%)	62 (92.5%)
Polypharmacy >=10	487 (47.4%)	2041 (63.6%)	7660 (61.7%)	85 (15.7%)	2195 (25.4%)	42 (62.7%)
Disease State						
Arthritis	202 (19.6%)	847 (26.4%)	2226 (17.9%)	268 (49.4%)	2634 (30.5%)	29 (43.3%)

Variable	IPCI N=1,028	CPRD GOLD N=3,211	SIDIAP N=12,410	EBB N=543	IQVIA DA Germany N=8,618	IQVIA LPD Belgium N=67
Atrial fibrillation	293 (28.5%)	807 (25.1%)	3323 (26.8%)	0 (0%)	1397 (16.2%)	0 (0%)
Chronic kidney disease	843 (82%)	2531 (78.8%)	10389 (83.7%)	454 (83.6%)	6902 (80%)	53 (79.1%)
Cerebrovascular disease	273 (26.6%)	648 (20.2%)	1722 (13.9%)	177 (32.6%)	2666 (30.9%)	15 (22.4%)
Diabetes	411 (40%)	1156 (36%)	5479 (44.1%)	179 (33%)	4122 (47.8%)	31 (46.3%)
Foot problems	0 (0%)	861 (26.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	223 (21.7%)	910 (28.3%)	3441 (27.7%)	168 (30.9%)	2328 (27%)	17 (25.4%)
Heart failure	260 (25.3%)	450 (14%)	3349 (27%)	394 (72.6%)	3155 (36.6%)	25 (37.3%)
Heart valve disease	114 (11.1%)	383 (11.9%)	2574 (20.7%)	51 (9.4%)	1719 (19.9%)	6 (9%)
Hypertension	682 (66.3%)	1707 (53.2%)	9867 (79.5%)	448 (82.5%)	7744 (89.8%)	63 (94%)
Hypotension	278 (27%)	565 (17.6%)	790 (6.4%)	14 (2.6%)	820 (9.5%)	10 (14.9%)
Ischaemic heart disease	349 (33.9%)	880 (27.4%)	2569 (20.7%)	348 (64.1%)	4237 (49.1%)	27 (40.3%)
Osteoporosis	159 (15.5%)	494 (15.4%)	2438 (19.6%)	107 (19.7%)	1979 (22.9%)	28 (41.8%)
Parkinsonism & tremor	27 (2.6%)	391 (12.2%)	1382 (11.1%)	57 (10.5%)	1337 (15.5%)	12 (17.9%)
Peptic ulcer	26 (2.5%)	161 (5%)	640 (5.2%)	196 (36.1%)	853 (9.9%)	6 (9%)
Peripheral vascular disease	193 (18.8%)	246 (7.7%)	1675 (13.5%)	100 (18.4%)	2378 (27.6%)	8 (11.9%)
Respiratory disease	450 (43.8%)	1686 (52.5%)	4507 (36.3%)	331 (61%)	5080 (58.9%)	49 (73.1%)
Skin ulcer	141 (13.7%)	145 (4.5%)	994 (8%)	33 (6.1%)	774 (9%)	NA (NA%)
Thyroid disease	158 (15.4%)	601 (18.7%)	2797 (22.5%)	198 (36.5%)	4626 (53.6%)	28 (41.8%)
Urinary system disease	588 (57.2%)	1386 (43.2%)	6690 (53.9%)	230 (42.4%)	3674 (42.6%)	32 (47.8%)
Symptoms/signs						
Dyspnoea	422 (41.1%)	2184 (68%)	2686 (21.6%)	16 (2.9%)	2054 (23.8%)	0 (0%)
Dizziness	373 (36.3%)	1418 (44.2%)	4106 (33.1%)	124 (22.8%)	3188 (37%)	15 (22.4%)

Variable	IPCI N=1,028	CPRD GOLD N=3,211	SIDIAP N=12,410	EBB N=543	IQVIA DA Germany N=8,618	IQVIA LPD Belgium N=67
Falls	0 (0%)	1185 (36.9%)	1735 (14%)	0 (0%)	0 (0%)	NA (NA%)
Memory & Cognitive problems	245 (23.8%)	535 (16.7%)	3050 (24.6%)	41 (7.6%)	1524 (17.7%)	12 (17.9%)
Sleep disturbance	425 (41.3%)	1115 (34.7%)	4496 (36.2%)	332 (61.1%)	3411 (39.5%)	53 (79.1%)
Urinary incontinence	467 (45.4%)	1172 (36.5%)	4642 (37.4%)	71 (13.1%)	2068 (24%)	16 (23.9%)
Weight loss & anorexia	320 (31.1%)	562 (17.5%)	1390 (11.2%)	6 (1.1%)	1042 (12.1%)	NA (NA%)
Disability						
Activity limitation	0 (0%)	28 (0.9%)	1193 (9.6%)	NA (NA%)	NA (NA%)	0 (0%)
Hearing impairment	217 (21.1%)	923 (28.7%)	3195 (25.7%)	212 (39%)	1598 (18.5%)	NA (NA%)
Housebound	0 (0%)	211 (6.6%)	1720 (13.9%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	328 (10.2%)	328 (2.6%)	NA (NA%)	375 (4.3%)	0 (0%)
Requiring care	0 (0%)	207 (6.4%)	1571 (12.7%)	0 (0%)	327 (3.8%)	0 (0%)
Social vulnerability	324 (31.5%)	173 (5.4%)	2688 (21.7%)	NA (NA%)	47 (0.5%)	NA (NA%)
Visual impairment	514 (50%)	1203 (37.5%)	8215 (66.2%)	376 (69.2%)	3176 (36.8%)	11 (16.4%)
Abnormal laboratory value						
Anaemia	374 (36.4%)	1039 (32.4%)	6595 (53.1%)	160 (29.5%)	3327 (38.6%)	20 (29.9%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

Table 17. Characteristics of Individuals with selected cancers within the Severe Frailty category, by databases.

Variable	IPCI N=121	CPRD GOLD N=623	SIDIAP N=4,603	EBB N=165	IQVIA DA Germany N=2,599	IQVIA LPD Belgium N=NA
Median Age	82	82	84	75	81	90
Age Group: 18 to 44	0 (0%)	NA (NA%)	NA (NA%)	NA (NA%)	0 (0%)	0 (0%)
Age Group: 45 to 64	NA (NA%)	27 (4.3%)	134 (2.9%)	14 (8.5%)	200 (7.7%)	0 (0%)
Age Group: 65 to 74	16 (13.2%)	123 (19.7%)	507 (11%)	61 (37%)	461 (17.7%)	NA (NA%)
Age Group: 75 to 84	63 (52.1%)	251 (40.3%)	1701 (37%)	67 (40.6%)	1171 (45%)	0 (0%)
Age Group: 85 to 120	39 (32.2%)	221 (35.5%)	2257 (49%)	22 (13.3%)	769 (29.6%)	NA (NA%)
Sex: Female	80 (66.1%)	406 (65.2%)	2725 (59.2%)	118 (71.5%)	1536 (59.1%)	NA (NA%)
Sex: Male	41 (33.9%)	217 (34.8%)	1878 (40.8%)	47 (28.5%)	1063 (40.9%)	NA (NA%)
Median frailty score	0.389	0.389	0.389	0.389	0.389	0.361
Median number of medications	11	14	13	8	9	8
Polypharmacy >=5	109 (90.1%)	614 (98.6%)	4538 (98.6%)	149 (90.3%)	2316 (89%)	5 (100%)
Polypharmacy >=10	73 (60.3%)	520 (83.5%)	3689 (80.1%)	43 (26.1%)	1068 (41.1%)	NA (NA%)
Disease State						
Arthritis	38 (31.4%)	238 (38.2%)	966 (21%)	110 (66.7%)	1189 (45.7%)	NA (NA%)
Atrial fibrillation	58 (47.9%)	239 (38.4%)	2138 (46.4%)	0 (0%)	734 (28.2%)	0 (0%)
Chronic kidney disease	109 (90.1%)	572 (91.8%)	4298 (93.4%)	158 (95.8%)	2440 (93.8%)	5 (100%)
Cerebrovascular disease	60 (49.6%)	206 (33.1%)	1200 (26.1%)	92 (55.8%)	1298 (49.9%)	NA (NA%)
Diabetes	71 (58.7%)	295 (47.4%)	2530 (55%)	86 (52.1%)	1634 (62.8%)	NA (NA%)
Foot problems	0 (0%)	272 (43.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	46 (38%)	278 (44.6%)	2072 (45%)	91 (55.2%)	1097 (42.2%)	NA (NA%)
Heart failure	55 (45.5%)	147 (23.6%)	2643 (57.4%)	145 (87.9%)	1644 (63.2%)	NA (NA%)

Variable	IPCI N=121	CPRD GOLD N=623	SIDIAP N=4,603	EBB N=165	IQVIA DA Germany N=2,599	IQVIA LPD Belgium N=NA
Heart valve disease	26 (21.5%)	132 (21.2%)	1809 (39.3%)	38 (23%)	842 (32.4%)	NA (NA%)
Hypertension	87 (71.9%)	394 (63.2%)	4089 (88.8%)	152 (92.1%)	2504 (96.3%)	5 (100%)
Hypotension	50 (41.3%)	210 (33.7%)	666 (14.5%)	8 (4.8%)	483 (18.6%)	0 (0%)
Ischaemic heart disease	56 (46.3%)	279 (44.8%)	1568 (34.1%)	134 (81.2%)	1822 (70%)	NA (NA%)
Osteoporosis	31 (25.6%)	168 (27%)	1455 (31.6%)	52 (31.5%)	1029 (39.6%)	NA (NA%)
Parkinsonism & tremor	5 (4.1%)	139 (22.3%)	905 (19.7%)	34 (20.6%)	718 (27.6%)	NA (NA%)
Peptic ulcer	NA (NA%)	45 (7.2%)	348 (7.6%)	84 (50.9%)	494 (19%)	0 (0%)
Peripheral vascular disease	38 (31.4%)	100 (16.1%)	989 (21.5%)	52 (31.5%)	1106 (42.5%)	NA (NA%)
Respiratory disease	60 (49.6%)	405 (65%)	2215 (48.1%)	129 (78.2%)	1869 (71.9%)	NA (NA%)
Skin ulcer	36 (29.8%)	63 (10.1%)	941 (20.4%)	15 (9.1%)	517 (19.9%)	0 (0%)
Thyroid disease	36 (29.8%)	182 (29.2%)	1390 (30.2%)	103 (62.4%)	1757 (67.6%)	NA (NA%)
Urinary system disease	79 (65.3%)	394 (63.2%)	3262 (70.9%)	95 (57.6%)	1579 (60.7%)	NA (NA%)
Symptoms/signs						
Dyspnoea	82 (67.8%)	519 (83.3%)	1768 (38.4%)	6 (3.6%)	1102 (42.4%)	0 (0%)
Dizziness	58 (47.9%)	402 (64.5%)	2094 (45.5%)	67 (40.6%)	1600 (61.5%)	NA (NA%)
Falls	0 (0%)	380 (61%)	1427 (31%)	0 (0%)	0 (0%)	0 (0%)
Memory & Cognitive problems	51 (42.1%)	201 (32.3%)	2102 (45.7%)	27 (16.4%)	865 (33.3%)	0 (0%)
Sleep disturbance	64 (52.9%)	325 (52.2%)	2257 (49%)	141 (85.5%)	1470 (56.5%)	NA (NA%)
Urinary incontinence	76 (62.8%)	345 (55.4%)	3035 (65.9%)	49 (29.7%)	1149 (44.2%)	NA (NA%)
Weight loss & anorexia	53 (43.8%)	205 (32.9%)	798 (17.3%)	9 (5.5%)	615 (23.6%)	0 (0%)
Disability						
Activity limitation	0 (0%)	8 (1.3%)	703 (15.3%)	0 (0%)	0 (0%)	0 (0%)

Variable	IPCI N=121	CPRD GOLD N=623	SIDIAP N=4,603	EBB N=165	IQVIA DA Germany N=2,599	IQVIA LPD Belgium N=NA
Hearing impairment	42 (34.7%)	253 (40.6%)	1611 (35%)	75 (45.5%)	893 (34.3%)	NA (NA%)
Housebound	0 (0%)	85 (13.6%)	1774 (38.5%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	147 (23.6%)	374 (8.1%)	0 (0%)	244 (9.4%)	0 (0%)
Requiring care	0 (0%)	94 (15.1%)	1593 (34.6%)	0 (0%)	181 (7%)	0 (0%)
Social vulnerability	68 (56.2%)	61 (9.8%)	1593 (34.6%)	NA (NA%)	21 (0.8%)	0 (0%)
Visual impairment	80 (66.1%)	335 (53.8%)	3598 (78.2%)	146 (88.5%)	1489 (57.2%)	NA (NA%)
Abnormal laboratory value						
Anaemia	76 (62.8%)	310 (49.8%)	3375 (73.3%)	95 (57.6%)	1568 (60.3%)	NA (NA%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

12.3.5 Characteristics of Individuals with Polypharmacy

Two thresholds of concomitant drug use were used to identify polypharmacy: >=5 and >=10 drugs. The characteristics of individuals with polypharmacy (using the >=5 threshold) are described in **Table 18**, while those of individuals with polypharmacy (using the >=10 threshold) are described in **Table 18**.

In terms of sex, there was a slight male predominance when the >=5 drugs threshold was used, while when using a >=10 drugs, there was a clear female predominance in some databases (IPCI, SIDIAP, and EBB, IQVIA LPD Belgium), while slight male predominance in the remaining (CPRD GOLD and IQVIA DA Germany). Regarding age, individuals with polypharmacy using the >=5 drugs threshold were generally within the 65-74 and 75-84 categories. Using the >=10 drugs polypharmacy threshold, most individuals were within the 75-84 and 85 and above category in almost all databases.

The median frailty score for individuals in the >=5 polypharmacy category ranged between 0.11-0.22, while among individuals in the >=10 polypharmacy category, it ranged between 0.14-0.28.

Within the >=5 drugs polypharmacy threshold, some conditions, such as chronic kidney disease, hypertension, and respiratory disease, had a prevalence of ~20% or above in all databases. Among the >=10 drugs polypharmacy category, the prevalence of conditions increased compared to >=5 drugs polypharmacy.

Table 18. Characteristics of individuals among all selected cancers with polypharmacy (using the >=5 drugs threshold).

Variable	IPCI N=10,645	CPRD GOLD N=29,905	SIDIAP N=60,150	EBB N=1,263	IQVIA DA Germany N=29,954	IQVIA LPD Belgium N=1,288
Median Age	73	73	74	70	75	71
Age Group: 18 to 44	126 (1.2%)	481 (1.6%)	1269 (2.1%)	40 (3.2%)	390 (1.3%)	54 (4.2%)
Age Group: 45 to 64	2235 (21%)	6371 (21.3%)	13148 (21.9%)	351 (27.8%)	6166 (20.6%)	328 (25.5%)
Age Group: 65 to 74	3711 (34.9%)	9739 (32.6%)	17447 (29%)	481 (38.1%)	8420 (28.1%)	391 (30.4%)
Age Group: 75 to 84	3383 (31.8%)	9518 (31.8%)	18190 (30.2%)	317 (25.1%)	10734 (35.8%)	375 (29.1%)
Age Group: 85 to 120	1190 (11.2%)	3796 (12.7%)	10093 (16.8%)	74 (5.9%)	4275 (14.3%)	140 (10.9%)
Sex: Female	5207 (48.9%)	14922 (49.9%)	27715 (46.1%)	597 (47.3%)	14122 (47.1%)	657 (51%)
Sex: Male	5438 (51.1%)	14983 (50.1%)	32435 (53.9%)	666 (52.7%)	15832 (52.8%)	631 (49%)
Median frailty score	0.111	0.111	0.167	0.222	0.194	0.111
Median number of medications	8	8	9	6	7	7
Disease State						
Arthritis	864 (8.1%)	4008 (13.4%)	8248 (13.7%)	529 (41.9%)	5506 (18.4%)	277 (21.5%)
Atrial fibrillation	1101 (10.3%)	3313 (11.1%)	8748 (14.5%)	0 (0%)	3197 (10.7%)	0 (0%)
Chronic kidney disease	4116 (38.7%)	11640 (38.9%)	34414 (57.2%)	819 (64.8%)	15567 (51.9%)	378 (29.3%)
Cerebrovascular disease	1108 (10.4%)	2615 (8.7%)	4842 (8%)	260 (20.6%)	5666 (18.9%)	115 (8.9%)
Diabetes	2153 (20.2%)	5730 (19.2%)	18816 (31.3%)	380 (30.1%)	11086 (37%)	296 (23%)
Foot problems	0 (0%)	2904 (9.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	819 (7.7%)	4011 (13.4%)	9906 (16.5%)	327 (25.9%)	4743 (15.8%)	75 (5.8%)
Heart failure	741 (7%)	1383 (4.6%)	7894 (13.1%)	686 (54.3%)	6750 (22.5%)	135 (10.5%)

Variable	IPCI N=10,645	CPRD GOLD N=29,905	SIDIAP N=60,150	EBB N=1,263	IQVIA DA Germany N=29,954	IQVIA LPD Belgium N=1,288
Heart valve disease	378 (3.6%)	1328 (4.4%)	6709 (11.2%)	99 (7.8%)	3475 (11.6%)	29 (2.3%)
Hypertension	4120 (38.7%)	10476 (35%)	36875 (61.3%)	935 (74%)	23275 (77.6%)	900 (69.9%)
Hypotension	1006 (9.5%)	1714 (5.7%)	2081 (3.5%)	24 (1.9%)	1450 (4.8%)	46 (3.6%)
Ischaemic heart disease	1643 (15.4%)	4063 (13.6%)	7786 (12.9%)	609 (48.2%)	9608 (32%)	168 (13%)
Osteoporosis	463 (4.3%)	1893 (6.3%)	7125 (11.8%)	138 (10.9%)	3838 (12.8%)	190 (14.8%)
Parkinsonism & tremor	100 (0.9%)	1328 (4.4%)	3803 (6.3%)	92 (7.3%)	2618 (8.7%)	78 (6.1%)
Peptic ulcer	118 (1.1%)	652 (2.2%)	1888 (3.1%)	325 (25.7%)	1786 (6%)	42 (3.3%)
Peripheral vascular disease	671 (6.3%)	1005 (3.4%)	4617 (7.7%)	162 (12.8%)	5101 (17%)	30 (2.3%)
Respiratory disease	2399 (22.5%)	8658 (29%)	15900 (26.4%)	638 (50.5%)	12320 (41.1%)	594 (46.1%)
Skin ulcer	421 (4%)	419 (1.4%)	2598 (4.3%)	52 (4.1%)	1691 (5.6%)	8 (0.6%)
Thyroid disease	652 (6.1%)	2773 (9.3%)	9532 (15.8%)	357 (28.3%)	10986 (36.6%)	202 (15.7%)
Urinary system disease	2315 (21.7%)	4495 (15%)	19896 (33.1%)	368 (29.1%)	7071 (23.6%)	138 (10.7%)
Symptoms/signs						
Dyspnoea	1656 (15.6%)	9596 (32.1%)	7415 (12.3%)	25 (2%)	3951 (13.2%)	6 (0.5%)
Dizziness	1317 (12.4%)	5032 (16.8%)	12883 (21.4%)	178 (14.1%)	6116 (20.4%)	104 (8.1%)
Falls	0 (0%)	3578 (12%)	4498 (7.5%)	0 (0%)	0 (0%)	9 (0.7%)
Memory & Cognitive problems	749 (7%)	1815 (6.1%)	7690 (12.8%)	64 (5.1%)	3067 (10.2%)	46 (3.6%)
Sleep disturbance	1665 (15.6%)	4287 (14.3%)	14810 (24.6%)	593 (47%)	7294 (24.3%)	524 (40.7%)
Urinary incontinence	1703 (16%)	4168 (13.9%)	11451 (19%)	112 (8.9%)	4134 (13.8%)	84 (6.5%)
Weight loss & anorexia	1138 (10.7%)	2008 (6.7%)	4194 (7%)	14 (1.1%)	2334 (7.8%)	11 (0.9%)

Variable	IPCI N=10,645	CPRD GOLD N=29,905	SIDIAP N=60,150	EBB N=1,263	IQVIA DA Germany N=29,954	IQVIA LPD Belgium N=1,288
Disability						
Activity limitation	0 (0%)	53 (0.2%)	3227 (5.4%)	NA (NA%)	NA (NA%)	0 (0%)
Hearing impairment	878 (8.2%)	3683 (12.3%)	9609 (16%)	323 (25.6%)	3016 (10.1%)	12 (0.9%)
Housebound	0 (0%)	681 (2.3%)	4044 (6.7%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	870 (2.9%)	863 (1.4%)	NA (NA%)	662 (2.2%)	0 (0%)
Requiring care	0 (0%)	800 (2.7%)	3840 (6.4%)	0 (0%)	641 (2.1%)	0 (0%)
Social vulnerability	1017 (9.6%)	532 (1.8%)	6960 (11.6%)	5 (0.4%)	81 (0.3%)	11 (0.9%)
Visual impairment	2273 (21.4%)	4815 (16.1%)	27165 (45.2%)	636 (50.4%)	6094 (20.3%)	109 (8.5%)
Abnormal laboratory value						
Anaemia	1483 (13.9%)	3852 (12.9%)	18873 (31.4%)	337 (26.7%)	7050 (23.5%)	134 (10.4%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

Table 19. Characteristics of individuals among all selected cancers with polypharmacy (using the >=10 drugs threshold).

Variable	IPCI N=3,552	CPRD GOLD N=11,954	SIDIAP N=24,454	EBB N=183	IQVIA DA Germany N=6,857	IQVIA LPD Belgium N=327
Median Age	75	75	77	72	77	73
Age Group: 18 to 44	14 (0.4%)	113 (0.9%)	185 (0.8%)	NA (NA%)	33 (0.5%)	8 (2.4%)
Age Group: 45 to 64	590 (16.6%)	2056 (17.2%)	3635 (14.9%)	30 (16.4%)	921 (13.4%)	67 (20.5%)
Age Group: 65 to 74	1171 (33%)	3749 (31.4%)	6578 (26.9%)	79 (43.2%)	1802 (26.2%)	103 (31.5%)
Age Group: 75 to 84	1316 (37%)	4200 (35.1%)	8752 (35.8%)	63 (34.4%)	2810 (40.9%)	108 (33%)
Age Group: 85 to 120	461 (13%)	1836 (15.4%)	5304 (21.7%)	8 (4.4%)	1305 (19%)	41 (12.5%)
Sex: Female	1661 (46.8%)	6113 (51.1%)	11024 (45.1%)	89 (48.6%)	3269 (47.6%)	167 (51.1%)
Sex: Male	1891 (53.2%)	5841 (48.9%)	13430 (54.9%)	94 (51.4%)	3588 (52.2%)	160 (48.9%)
Median frailty score	0.139	0.167	0.222	0.278	0.222	0.139
Median number of medications	12	12	12	11	11	12
Disease State						
Arthritis	313 (8.8%)	1806 (15.1%)	3787 (15.5%)	83 (45.4%)	1439 (20.9%)	73 (22.3%)
Atrial fibrillation	475 (13.4%)	1677 (14%)	5332 (21.8%)	0 (0%)	1060 (15.4%)	0 (0%)
Chronic kidney disease	1610 (45.3%)	5526 (46.2%)	16398 (67.1%)	141 (77%)	4179 (60.8%)	119 (36.4%)
Cerebrovascular disease	460 (13%)	1359 (11.4%)	2819 (11.5%)	49 (26.8%)	1612 (23.5%)	35 (10.7%)
Diabetes	911 (25.6%)	3092 (25.9%)	10718 (43.8%)	85 (46.4%)	3518 (51.2%)	105 (32.1%)
Foot problems	0 (0%)	1709 (14.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	315 (8.9%)	2012 (16.8%)	5198 (21.3%)	57 (31.1%)	1504 (21.9%)	24 (7.3%)
Heart failure	407 (11.5%)	848 (7.1%)	5517 (22.6%)	125 (68.3%)	2411 (35.1%)	62 (19%)

Variable	IPCI N=3,552	CPRD GOLD N=11,954	SIDIAP N=24,454	EBB N=183	IQVIA DA Germany N=6,857	IQVIA LPD Belgium N=327
Heart valve disease	151 (4.3%)	684 (5.7%)	4096 (16.7%)	16 (8.7%)	1035 (15.1%)	9 (2.8%)
Hypertension	1393 (39.2%)	4297 (35.9%)	17606 (72%)	148 (80.9%)	5759 (83.8%)	266 (81.3%)
Hypotension	413 (11.6%)	906 (7.6%)	1234 (5%)	NA (NA%)	392 (5.7%)	12 (3.7%)
Ischaemic heart disease	714 (20.1%)	2295 (19.2%)	5385 (22%)	111 (60.7%)	2900 (42.2%)	60 (18.3%)
Osteoporosis	182 (5.1%)	1091 (9.1%)	3856 (15.8%)	24 (13.1%)	1227 (17.9%)	69 (21.1%)
Parkinsonism & tremor	40 (1.1%)	748 (6.3%)	2259 (9.2%)	20 (10.9%)	827 (12%)	24 (7.3%)
Peptic ulcer	41 (1.2%)	340 (2.8%)	948 (3.9%)	61 (33.3%)	497 (7.2%)	13 (4%)
Peripheral vascular disease	336 (9.5%)	609 (5.1%)	3058 (12.5%)	42 (23%)	1790 (26.1%)	16 (4.9%)
Respiratory disease	1072 (30.2%)	4630 (38.7%)	8992 (36.8%)	120 (65.6%)	3275 (47.7%)	190 (58.1%)
Skin ulcer	214 (6%)	236 (2%)	1611 (6.6%)	9 (4.9%)	726 (10.6%)	NA (NA%)
Thyroid disease	253 (7.1%)	1327 (11.1%)	4596 (18.8%)	60 (32.8%)	2786 (40.5%)	73 (22.3%)
Urinary system disease	911 (25.6%)	2253 (18.8%)	9598 (39.2%)	70 (38.3%)	1945 (28.3%)	40 (12.2%)
Symptoms/signs						
Dyspnoea	732 (20.6%)	5323 (44.5%)	4318 (17.7%)	6 (3.3%)	1227 (17.9%)	0 (0%)
Dizziness	498 (14%)	2424 (20.3%)	6117 (25%)	35 (19.1%)	1689 (24.6%)	43 (13.1%)
Falls	0 (0%)	1908 (16%)	2469 (10.1%)	0 (0%)	0 (0%)	NA (NA%)
Memory & Cognitive problems	300 (8.4%)	972 (8.1%)	4175 (17.1%)	19 (10.4%)	1052 (15.3%)	19 (5.8%)
Sleep disturbance	679 (19.1%)	2273 (19%)	7656 (31.3%)	117 (63.9%)	2126 (30.9%)	162 (49.5%)
Urinary incontinence	681 (19.2%)	2069 (17.3%)	6540 (26.7%)	23 (12.6%)	1491 (21.7%)	25 (7.6%)
Weight loss & anorexia	446 (12.6%)	1034 (8.6%)	2047 (8.4%)	NA (NA%)	676 (9.8%)	7 (2.1%)

Variable	IPCI N=3,552	CPRD GOLD N=11,954	SIDIAP N=24,454	EBB N=183	IQVIA DA Germany N=6,857	IQVIA LPD Belgium N=327
Disability						
Activity limitation	0 (0%)	32 (0.3%)	1934 (7.9%)	NA (NA%)	NA (NA%)	0 (0%)
Hearing impairment	353 (9.9%)	1684 (14.1%)	4625 (18.9%)	48 (26.2%)	784 (11.4%)	6 (1.8%)
Housebound	0 (0%)	440 (3.7%)	2580 (10.6%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	560 (4.7%)	522 (2.1%)	0 (0%)	239 (3.5%)	0 (0%)
Requiring care	0 (0%)	533 (4.5%)	2339 (9.6%)	0 (0%)	237 (3.4%)	0 (0%)
Social vulnerability	433 (12.2%)	296 (2.5%)	3559 (14.6%)	NA (NA%)	16 (0.2%)	NA (NA%)
Visual impairment	895 (25.2%)	2394 (20%)	13456 (55%)	115 (62.8%)	1708 (24.9%)	35 (10.7%)
Abnormal laboratory value						
Anaemia	697 (19.6%)	2086 (17.5%)	10179 (41.6%)	66 (36.1%)	2242 (32.6%)	46 (14.1%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

12.3.6 One-Year Hospitalisation and Mortality

Table 20 displays each database's one-year average number of hospitalisations by frailty and polypharmacy categories. Hospitalisation data was only available for SIDIAP and EBB. A rate >1 indicates that the number of hospitalisations exceeded the number of individuals within that category, due to recurrent hospitalisations in some subjects. Hospitalisation ranged from fit to severely frail, between 1.18-1.54 in SIDIAP and 3.33-3.71 in EBB.

SIDIAP had a clear positive gradient between hospitalisation rate and frailty and polypharmacy severity category.

Table 20. One-year Hospitalisation Rate (%) in selected cancers, by frailty and polypharmacy categories.

Database	Rate	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
SIDIAP	one-year Hospitalisation rate	1.18	1.39	1.52	1.54	1.36	1.46
EBB	one-year Hospitalisation rate	3.33	3.41	3.30	3.71	3.47	4.00

All values are N (%) unless otherwise stated. NA=Count <5.

Table 21 displays each database's one-year mortality risk by frailty and polypharmacy categories. Mortality data was only available for IPCI, CPRD GOLD, SIDIAP, and EBB. All databases exhibited a positive gradient between mortality rate and the increasing severity of frailty and polypharmacy. The one-year mortality rate ranged between 13-25% among fit individuals and 35-72% among severely frail individuals.

Table 21. One-year Mortality risk in selected cancers, by frailty and polypharmacy categories.

Database	Rate	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
IPCI	one-year Mortality risk	0.25	0.41	0.50	0.58	0.40	0.48
CPRD GOLD	one-year Mortality risk	0.25	0.42	0.52	0.57	0.42	0.51
SIDIAP	one-year Mortality risk	0.21	0.37	0.56	0.72	0.41	0.51
EBB	one-year Mortality risk	0.13	0.19	0.26	0.35	0.24	0.28

12.4 Large-scale Characterization

A large-scale characterisation of conditions, observations, procedures, signs, and symptoms and drug use summarised the characteristics of individuals included in the study by database and at different time windows. In this report, we present the results for the window of 365-31 days before the index date, by database, for the overall cohort of individuals with selected cancers for conditions in

Table 22 and drugs in **Table 23**.

Conditions related to hypertension, blood pressure findings, and heart disease were among the top 10 conditions in all databases. Respiratory system-related conditions, such as cough, Dyspnoea, and chronic obstructive respiratory disease, were also among the top 10 conditions.

Influenza and SARS-CoV-2 vaccination were among the 10 most common prescriptions in all databases, along with proton pump inhibitors, insulin sensitisers (metformin), blood pressure medications (calcium channel blockers, beta-blockers, diuretics), and analgesics (dipyrone and acetaminophen), among others.

Table 22. Large-scale characterisation of the 10 most prevalent conditions, observations, procedures, signs, and symptoms by database for the 365-31 days before the index date window of incident selected cancer diagnosis.

Rank (time_window: -365 to -31)	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
1	Essential hypertension [n=2971, 12.2%]	Blood pressure finding [n=31806, 58.4%]	Traumatic or non-traumatic injury [n=10910, 10.2%]	Essential hypertension [n=855, 25.8%]	Essential hypertension [n=21224, 13.4%]	Essential hypertension [n=976, 32.9%]
2	Cough [n=2220, 9.1%]	Finding of pulse rate [n=9534, 17.5%]	Low back pain [n=10635, 9.9%]	Hyperplasia of prostate [n=789, 23.8%]	Illness [n=8239, 5.2%]	Pure hypercholesterolemia [n=567, 19.1%]
3	Excessive cerumen in ear canal [n=2185, 9%]	Patient self-report [n=4917, 9%]	Essential hypertension [n=8245, 7.7%]	Hypertensive heart disease without congestive heart failure [n=785, 23.7%]	Nerve root disorder [n=7401, 4.7%]	Disorders of initiating and maintaining sleep [n=364, 12.3%]
4	Type 2 diabetes mellitus [n=2076, 8.5%]	Exercise grading [n=4688, 8.6%]	Urinary tract infectious disease [n=8033, 7.5%]	Serum cholesterol raised [n=400, 12.1%]	Hyperplasia of prostate [n=7327, 4.6%]	Type 2 diabetes mellitus without complication [n=286, 9.6%]
5	Urinary tract infectious disease [n=1691, 6.9%]	Cough [n=4135, 7.6%]	Common cold [n=6874, 6.4%]	Hypertensive heart disease [n=363, 11%]	Type 2 diabetes mellitus without complication [n=6237, 3.9%]	Depressive disorder [n=279, 9.4%]

Rank (time_window: -365 to -31)	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
6	Fatigue [n=1498, 6.1%]	No response to bowel cancer screening programme invitation [n=3664, 6.7%]	Abdominal pain [n=6654, 6.2%]	Acute upper respiratory infection [n=331, 10%]	Acute upper respiratory infection [n=5413, 3.4%]	Low back pain [n=256, 8.6%]
7	Finding of region of thorax [n=1425, 5.8%]	Abdominal pain [n=2329, 4.3%]	Pain of knee region [n=6644, 6.2%]	Hypertensive heart disease with congestive heart failure [n=320, 9.7%]	Pure hypercholesterolemia [n=4726, 3%]	Gastroesophageal reflux disease [n=256, 8.6%]
8	10g monofilament sensation R foot normal [n=1361, 5.6%]	Breast lump [n=2147, 3.9%]	Joint pain [n=6405, 6%]	Disorder of lipid metabolism [n=317, 9.6%]	Urinary tract infectious disease [n=4458, 2.8%]	Chronic obstructive lung disease [n=226, 7.6%]
9	10g monofilament sensation L foot normal [n=1353, 5.5%]	Dyspnoea [n=1623, 3%]	Cough [n=5974, 5.6%]	Atrial arrhythmia [n=308, 9.3%]	Chronic obstructive lung disease [n=4265, 2.7%]	Cough [n=212, 7.2%]
10	Fit and well [n=1340, 5.5%]	10g monofilament sensation L foot normal [n=1589, 2.9%]	Acute lower respiratory tract infection [n=5247, 4.9%]	Nerve root disorder [n=289, 8.7%]	Chronic ischaemic heart disease [n=3721, 2.4%]	Esophagitis [n=201, 6.8%]

All values are N (%) unless otherwise stated. NA=Count <5.

Table 23. Large-scale characterisation of the 10 most prevalent drugs used by database for the 365-31 days before the index date window.

Rank (time_window: -365 to -31)	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
1	aspirin 80 MG Oral Tablet [n=2686, 11%]	influenza virus vaccine, unspecified formulation [n=15418, 28.3%]	Influenza, seasonal, injectable [n=37356, 34.9%]	SARS-COV-2 (COVID-19) vaccine, UNSPECIFIED [n=563, 17%]	Influenza, seasonal, injectable [n=37356, 34.9%]	Aspirin 81 MG Delayed Release Oral Capsule, [n=450, 15.18%]
2	omeprazole 20 MG Delayed Release Oral Capsule [n=2405, 9.9%]	omeprazole 20 MG Delayed Release Oral Capsule [n=11827, 21.7%]	omeprazole 20 MG Delayed Release Oral Capsule [n=37010, 34.6%]	SARS-CoV-2 (COVID-19) vaccine, mRNA-BNT162b2 0.1 MG/ML Injectable Suspension [n=538, 16.3%]	omeprazole 20 MG Delayed Release Oral Capsule [n=37010, 34.6%]	SARS-CoV-2 (COVID-19) vaccine, mRNA spike protein [n=408, 13.77%]
3	SARS-CoV-2 (COVID-19) vaccine, mRNA-BNT162b2 0.1 MG/ML Injectable Suspension [n=2093, 8.6%]	amoxicillin 500 MG Oral Capsule [n=7981, 14.7%]	acetaminophen 1000 MG Oral Tablet [n=34169, 31.9%]	metoprolol succinate 50 MG Extended Release Oral Tablet [n=366, 11.1%]	acetaminophen 1000 MG Oral Tablet [n=34169, 31.9%]	Influenza, injectable, quadrivalent, preservative free [n=231, 7.79%]
4	influenza A virus (H1N1) antigen / influenza A virus (H3N2) antigen / influenza B virus antigen Injectable Suspension [n=2058, 8.4%]	SARS-CoV-2 (COVID-19) vaccine, mRNA-BNT162b2 0.1 MG/ML Injectable Suspension [n=7400, 13.6%]	dipyrone [n=18886, 17.6%]	ciprofloxacin 500 MG Oral Tablet [n=348, 10.5%]	dipyrone [n=18886, 17.6%]	pantoprazole 20 MG Delayed Release Oral Capsule, [n=166, 5.6%]
5	polyethylene glycol 3350 13100 MG / potassium chloride 46.6 MG / sodium bicarbonate 179 MG / sodium chloride 351 MG Powder for Oral Solution [n=1918, 7.9%]	acetaminophen 500 MG Oral Tablet [n=6920, 12.7%]	SARS-CoV-2 (COVID-19) vaccine, mRNA-BNT162b2 0.1 MG/ML Injectable Suspension [n=14162, 13.2%]	Omeprazole 20 MG Oral Capsule [n=317, 9.6%]	SARS-CoV-2 (COVID-19) vaccine, mRNA-BNT162b2 0.1 MG/ML Injectable Suspension [n=14162, 13.2%]	pantoprazole 40 MG Delayed Release Oral Capsule, [n=128, 4.32%]

Rank (time_window: -365 to -31)	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
6	pantoprazole 40 MG Delayed Release Oral Tablet [n=1923, 7.9%]	aspirin 75 MG Disintegrating Oral Tablet [n=6134, 11.3%]	lorazepam 1 MG Oral Tablet [n=12445, 11.6%]	tamsulosin hydrochloride 0.4 MG Oral Capsule [n=313, 9.5%]	lorazepam 1 MG Oral Tablet [n=12445, 11.6%]	1 ML Cholecalciferol 25000 UNT/ML Injectable Solution, [n=122, 4.12%]
7	metformin hydrochloride 500 MG Oral Tablet [n=1807, 7.4%]	amlodipine 5 MG Oral Tablet [n=5926, 10.9%]	metformin hydrochloride 850 MG Oral Tablet [n=11901, 11.1%]	amoxicillin 875 MG / clavulanate 125 MG Oral Tablet [n=311, 9.4%]	metformin hydrochloride 850 MG Oral Tablet [n=11901, 11.1%]	Influenza, seasonal, injectable [n=91, 3.07%]
8	metoprolol succinate 50 MG Extended Release Oral Tablet [n=1781, 7.3%]	SARS-COV-2 (COVID-19) vaccine, vector non-replicating, recombinant spike protein-ChAdOx1, preservative free, 0.5 mL (non-US) [n=5898, 10.8%]	simvastatin 20 MG Oral Tablet [n=11422, 10.7%]	zopiclone 7.5 MG Oral Tablet [n=278, 8.4%]	simvastatin 20 MG Oral Tablet [n=11422, 10.7%]	rosuvastatin 10 MG Oral Tablet, [n=90, 3.04%]
9	Simvastatin 40 MG Delayed Release Oral Tablet [n=1682, 6.9%]	doxycycline hyclate 100 MG Oral Capsule [n=4977, 9.1%]	aspirin 100 MG Delayed Release Oral Tablet [n=11428, 10.7%]	nebivolol 5 MG Oral Tablet [n=228, 6.9%]	aspirin 100 MG Delayed Release Oral Tablet [n=11428, 10.7%]	zolpidem 10 MG Oral Tablet, [n=88, 2.97%]
10	hydrochlorothiazide 12.5 MG Oral Tablet [n=1683, 6.9%]	tamsulosin 0.4 MG Extended Release Oral Capsule [n=4868, 8.9%]	SARS-CoV-2 (COVID-19) vaccine, mRNA-1273 0.2 MG/ML Injectable Suspension [n=11006, 10.3%]	acetaminophen 500 MG / codeine phosphate 30 MG Oral Tablet [n=212, 6.4%]	SARS-CoV-2 (COVID-19) vaccine, mRNA-1273 0.2 MG/ML Injectable Suspension [n=11006, 10.3%]	Metformin 850 MG Delayed Release Oral Tablet, [n=84, 2.83%]

All values are N (%) unless otherwise stated. NA=Count <5.

12.5 Stratified Analyses

12.5.1 Characterization of frailty and polypharmacy by age, with a focus on older adults (aged 65 and above)

Age stratification in this report is focused on individuals aged >=65. Tables with full age groups are provided in **Appendix II. Table 2, Appendix II. Table 3, and**

Appendix II. Table 4.

Among all databases, among 65-and-over age groups, there was a male predominance until the 85 years and above age group, after which, for most databases, a female predominance was observed (except for IQVIA LPD Belgium) (**Table 24**).

Prevalence of Frailty and Polypharmacy in older adults (aged >=65)

The proportion of individuals with frailty increased with age. Frailty (understood as mild, moderate, and severe categories combined) ranged between 22.6-70.2% among those aged 65-74, between 31.7-82.7% among those aged 75-84, and between 39.9-92.3% among those aged 85 and above. Prevalence of frailty categories by age group was as follows (except for IQVIA LPD Belgium, where counts were low): mild frailty ranged between 17-42.7%, 20.7-41.7%, and. 26-41.3% in the 65-74, 75-84, and 85 and above age groups, respectively; moderate frailty ranged between 1.8-20.5%, 3.2-33%, and 7-41.5% in the 65-74, 75-84, and 85 and above age groups, respectively; and last, severe frailty ranged between 0.2-6%, 1.1-11.7%, and 2.2-19.1% in the 65-74, 75-84, and 85 and above age groups.

With increasing age, the proportion of individuals with greater frailty severity increased within each database. However, increments differed in each database. In this sense, in IPCI, for example, moderate frailty was 1.8% in the 65-74 age group and increased to 7.0% in the 85 and above age group, while in EBB, moderate frailty was 20.5% in the 65-74 age group and increased to 41.5% in the 85 and above age group. Similarly, severe frailty went 0.2% to 2.2 in IPCI, and 1.8 to 19.1 in SIDIAP, between the 65-74 and 85 and above age groups. This was also observed between databases (except for IQVIA LPD Belgium, where counts were low), where severe frailty ranged between 0.2 and 6% among those aged 65-74, between 1.1 and 11.7% in the 74-84 group, while severe frailty ranged between 2.2 and 16.9%.

In terms of polypharmacy, using the >5 drugs threshold, polypharmacy increased with age. Among those aged 65-74, polypharmacy ranged between 19.4-62.6%, between 25-79.4% in those 75-84, and between 38-85.6% in those 85 and above (among all databases, the lowest prevalence of polypharmacy was observed in IQVIA DA Germany, while the highest in SIDIAP).

Table 24. Demographic characteristics and prevalence of frailty and polypharmacy in older adults (>=65 years).

Variable	IPCI N=15,296	CPRD GOLD N=35,095	SIDIAP N=62,554	EBB N=1,723	IQVIA DA Germany N=97,587	IQVIA LPD Belgium N=1,809
Age group: 65 to 74						
Median Age	70	70	70	69	69	70
Sex: Female	3729 (46.7%)	7705 (44.7%)	11104 (39.9%)	466 (45.7%)	19119 (44%)	395 (47.6%)
Sex: Male	4263 (53.3%)	9551 (55.3%)	16758 (60.1%)	554 (54.3%)	24336 (56%)	434 (52.4%)

Variable	IPCI N=15,296	CPRD GOLD N=35,095	SIDIAP N=62,554	EBB N=1,723	IQVIA DA Germany N=97,587	IQVIA LPD Belgium N=1,809
Median frailty score	0.083	0.083	0.111	0.167	0.056	0.083
Frailty category: Fit	6187 (77.4%)	12321 (71.4%)	15075 (54.1%)	314 (30.8%)	33447 (76.9%)	614 (74.1%)
Frailty Category: Mild	1561 (19.5%)	4059 (23.5%)	9780 (35.1%)	436 (42.7%)	7454 (17.1%)	199 (24%)
Frailty category: Moderate	228 (2.9%)	753 (4.4%)	2500 (9%)	209 (20.5%)	2110 (4.9%)	15 (1.8%)
Frailty category: Severe	16 (0.2%)	123 (0.7%)	507 (1.8%)	61 (6%)	461 (1.1%)	NA (NA%)
Median number of medications	4	5	6	4	1	4
Polypharmacy >=5	3711 (46.4%)	9739 (56.4%)	17447 (62.6%)	481 (47.2%)	8420 (19.4%)	391 (47.2%)
Polypharmacy >=10	1171 (14.7%)	3749 (21.7%)	6578 (23.6%)	79 (7.7%)	1802 (4.1%)	103 (12.4%)
Age group: 75 to 84						
Median Age	79	79	79	78	79	79
Sex: Female	2499 (45.1%)	6001 (45.8%)	9812 (42.9%)	261 (45.5%)	18537 (43.2%)	296 (43.4%)
Sex: Male	3046 (54.9%)	7098 (54.2%)	13085 (57.1%)	312 (54.5%)	24372 (56.8%)	386 (56.6%)
Median frailty score	0.111	0.111	0.167	0.222	0.083	0.111
Frailty category: Fit	3220 (58.1%)	6943 (53%)	6732 (29.4%)	99 (17.3%)	29345 (68.3%)	423 (62%)
Frailty Category: Mild	1801 (32.5%)	4568 (34.9%)	9559 (41.7%)	218 (38%)	8906 (20.7%)	237 (34.8%)
Frailty category: Moderate	461 (8.3%)	1337 (10.2%)	4905 (21.4%)	189 (33%)	3515 (8.2%)	22 (3.2%)
Frailty category: Severe	63 (1.1%)	251 (1.9%)	1701 (7.4%)	67 (11.7%)	1171 (2.7%)	0 (0%)
Median number of medications	6	7	8	5	1	5
Polypharmacy >=5	3383 (61%)	9518 (72.7%)	18190 (79.4%)	317 (55.3%)	10734 (25%)	375 (55%)

Variable	IPCI N=15,296	CPRD GOLD N=35,095	SIDIAP N=62,554	EBB N=1,723	IQVIA DA Germany N=97,587	IQVIA LPD Belgium N=1,809
Polypharmacy >=10	1316 (23.7%)	4200 (32.1%)	8752 (38.2%)	63 (11%)	2810 (6.5%)	108 (15.8%)
Age group: 85 to 120						
Median Age	88	88	88	87	87	88
Sex: Female	946 (53.8%)	2526 (53.3%)	6330 (53.7%)	74 (56.9%)	5618 (50%)	138 (46.3%)
Sex: Male	813 (46.2%)	2214 (46.7%)	5465 (46.3%)	56 (43.1%)	5605 (49.9%)	160 (53.7%)
Median frailty score	0.139	0.167	0.25	0.25	0.111	0.111
Frailty category: Fit	726 (41.3%)	1774 (37.4%)	1598 (13.5%)	10 (7.7%)	5872 (52.3%)	179 (60.1%)
Frailty Category: Mild	727 (41.3%)	1914 (40.4%)	4064 (34.5%)	44 (33.8%)	2916 (26%)	94 (31.5%)
Frailty category: Moderate	267 (15.2%)	831 (17.5%)	3876 (32.9%)	54 (41.5%)	1679 (14.9%)	21 (7%)
Frailty category: Severe	39 (2.2%)	221 (4.7%)	2257 (19.1%)	22 (16.9%)	769 (6.8%)	NA (NA%)
Median number of medications	6	8	9	5	3	4
Polypharmacy >=5	1190 (67.7%)	3796 (80.1%)	10093 (85.6%)	74 (56.9%)	4275 (38%)	140 (47%)
Polypharmacy >=10	461 (26.2%)	1836 (38.7%)	5304 (45%)	8 (6.2%)	1305 (11.6%)	41 (13.8%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

The distribution of frailty conditions by age is available in the Shiny app (https://data-dev.darwin-eu.org/P2-C1-009-FrailtyPolypharmacyCancer/). Similar to the overall population, most conditions increased their prevalence with increasing frailty within each age group.

One-year Hospitalisations rate and Mortality risk in older adults

Table 25 and **Table 26** display the one-year hospitalisations and mortality, respectively. Within each age group, hospitalisation increased with increasing severity of frailty and polypharmacy categories; however, within each frailty category, hospitalisation seemed to decrease with increasing age, except for severe frailty and moderate, severe, and polypharmacy in EBB, where there was no clear pattern.

In terms of one-year mortality, risks increased within each age group with increasing severity of frailty and polypharmacy categories. The same was observed within each frailty category with the increase in age.

Table 25. One-year Hospitalisation Rate (%) in selected cancers, by frailty, polypharmacy, and age groups, in Older Adults (aged >=65).

Database	Hospitalisation Rate	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
SIDIAP	65-74	1.10	1.44	1.73	2.09	1.37	1.53
	75-84	0.95	1.29	1.56	1.68	1.32	1.44
	85+	0.79	1.02	1.18	1.27	1.11	1.16
EBB	65-74	2.77	3.19	3.41	4.06	3.33	3.85
	75-84	2.67	2.40	3.20	3.43	2.86	3.92
	85+	1.33	2.66	3.24	3.21	3.36	2.43

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

Table 26. One-year mortality risk in selected cancers, by frailty, polypharmacy, and age groups in older adults (aged >=65).

Database	Mortality Rate	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
IPCI	65-74	0.26	0.34	0.43	NA	0.34	0.42
	75-84	0.39	0.45	0.51	0.56	0.46	0.53
	85+	0.56	0.61	0.60	0.75	0.62	0.68
CPRD GOLD	65-74	0.25	0.36	0.41	0.50	0.36	0.46
	75-84	0.37	0.48	0.54	0.59	0.48	0.55
	85+	0.57	0.59	0.64	0.63	0.61	0.66
SIDIAP	65-74	0.24	0.31	0.42	0.57	0.33	0.39
	75-84	0.34	0.42	0.54	0.67	0.46	0.52
	85+	0.57	0.66	0.74	0.81	0.71	0.75
EBB	65-74	0.17	0.21	0.19	0.25	0.22	0.25
	75-84	0.25	0.23	0.32	0.35	0.30	0.36
	85+		0.74	0.62	0.79	0.73	

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage.

12.5.2. Patient Characteristics and Prevalence of Frailty and Polypharmacy by Sex

Full tables for this section are provided in **Appendix II**.

Appendix II. Table 5 displays the patient's characteristics and prevalence of frailty and polypharmacy by sex. Across all databases, women had a lower median age compared to men. The median age in women ranged between 63 years in EBB to 67 in IPCI and CPRD GOLD. The proportion of fit individuals ranged between 38.9% (EBB) and 76.7% (IQVIA DA Germany) for women and between 44.8% (EBB) to 76.8% (IPCI) in men. Within each database, the proportion of individuals was similar by sex, except for EBB, in which the proportion of fit men was higher than women. Similarly, the prevalence of frailty (understood as all individuals with mild, moderate, or severe) varied slightly by sex within each database, except for EBB, in which the prevalence of frailty was higher among women.

Among individual frailty categories, a slightly higher proportion of women was observed with increasing frailty severity.

The prevalence of polypharmacy (>=5 threshold) was greater in men than women and ranged between 20.3% (IQVIA DA Germany) and 60.3% (SIDIAP) in men. However, the prevalence of polypharmacy using the >=10 threshold did not show a clear predominance by sex, except for IPCI, in which the prevalence was higher for men (16.3%) compared to women (13.0%).

Appendix II. Table 6 displays the conditions included in the frailty score by sex. As expected, several conditions showed variation by sex within each database. In this sense, conditions such as chronic kidney disease, fragility fracture, osteoporosis, and thyroid disease predominated in women, while cerebrovascular disease, hypertension, ischaemic heart disease, and peripheral vascular disease predominated in males.

Characteristics of individual frailty categories are displayed by sex and database for fit (**Appendix II. Table 7**), mild (**Appendix II. Table 8**), moderate(**Appendix II. Table 9**)**,** and severe frailty (**Appendix II. Table 10**).

Regarding differences by sex among fit (**Appendix II. Table 7**) and mildly frail (**Appendix II. Table 8)** individuals, fit women tended to be younger than men. Among the moderate, differences by age concentrated among the older age groups. Among moderate frailty individuals, the proportion of men 75-84 was greater than that of women, while the opposite was observed in the 85 and above category (**Appendix II. Table 9).** The numbers were small for severe frailty (**Appendix II. Table 10)**. Age-wise, the proportion of women 85 and above was greater than that of men in almost all databases; for other age groups, results were inconsistent across databases.

The differences in the prevalence of conditions by sex were generally similar to those described above for the overall differences by sex, although they seemed to narrow or reverse for some conditions and databases with greater frailty severity, such as chronic kidney disease and hypertension (**Appendix II. Table 11**, **Appendix II. Table 12**, **Appendix II. Table 13**, **Appendix II. Table 14**).

Differences in Polypharmacy by sex

Regarding polypharmacy, using the >=5 drugs threshold, age distribution varied by sex. The proportion of women was higher than men for all age groups under 65 and 85 and above, while the opposite was observed for the 65-74 and 75-84 age groups (**Appendix II. Table 15**).

The differences in the prevalence of conditions by sex among individuals with polypharmacy were generally similar to those described above for the overall differences by sex (**Appendix II. Table 16**).

One-year hospitalisation and mortality by sex

The one-year hospitalisation rate(**Appendix II. Table 17**) was greater in males in SIDIAP, among the moderate and severe frailty categories, and polypharmacy (>=10 drugs). However, in EBB, the hospitalisation rate was higher among women for all categories compared to men, except for severe frailty, where it was greater for women.

One-year mortality risk was generally greater in men throughout all categories and databases (except for the severe frailty category in CPRD GOLD, in which mortality was higher in women) (

Appendix II. Table 18).

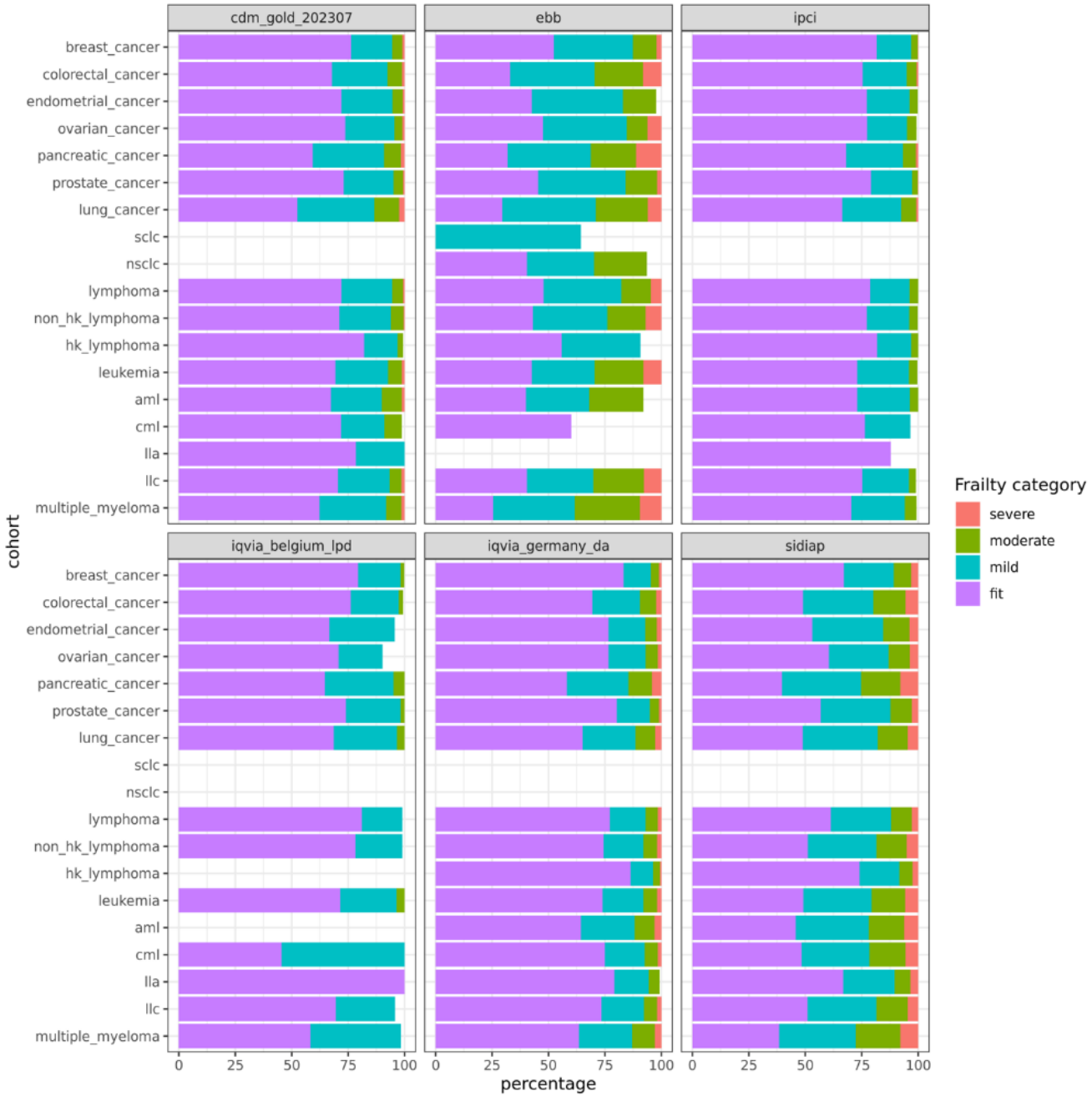
12.5.3 Prevalence of Frailty and Polypharmacy by Cancer Type

The Shiny app provides results for each cancer type by age, sex, and frailty category (https://data-dev.darwin-eu.org/P2-C1-009-FrailtyPolypharmacyCancer/).

Here, we describe the distribution of cases by cancer type, overall prevalence of frailty and polypharmacy by cancer type. Overall, the 4 most common cancer types in all databases were Breast, Colorectal, Prostate, and Lung cancer (**Appendix II. Table 1**). Each cancer type showed distinct age and sex characteristics. Age-wise, among different cancer types and databases, individuals with breast cancer were generally younger, while Multiple Myeloma patients were generally older compared to other cancer types. In terms of median frailty score by cancer type, the cancers with the highest median frailty score were Lung cancer (0.09-0.18), Pancreatic cancer (0.09-0.18), and Multiple Myeloma (0.09-0.21) (**Appendix II. Table 19**). Similarly, by frailty categories (fit, mild, moderate, and severe), these same cancer types exhibited the lowest prevalence of fit individuals and higher prevalence of more severe frailty categories across all databases (

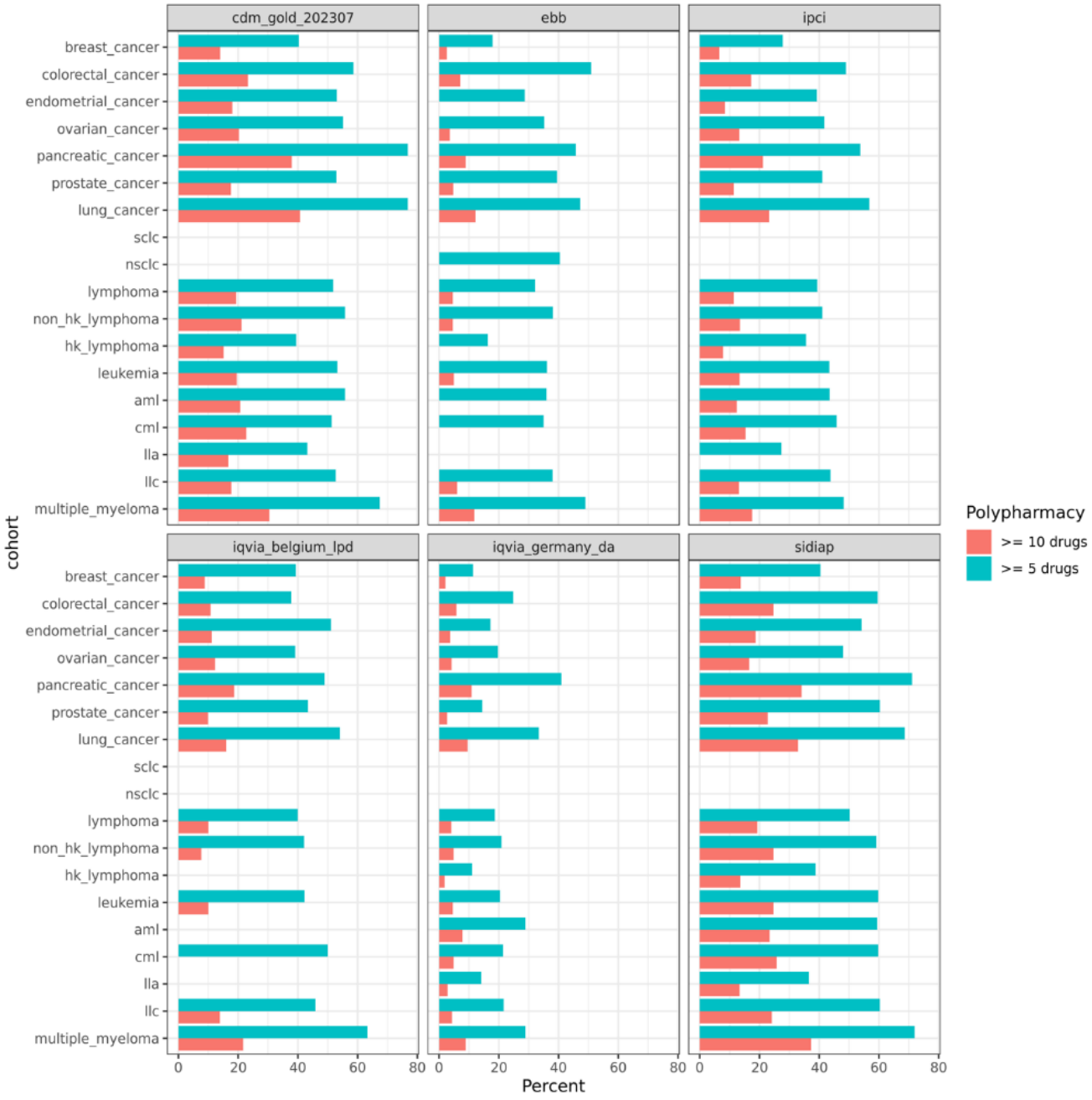
Figure 1). This was also the case for polypharmacy, using both thresholds and in almost all databases (**Figure 2**).

Figure 1. Prevalence of frailty categories by cancer type.



All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD; iqvia_belgium_lpd=IQVIA LPD Belgium; iqvia_germany_da=IQVIA DA Germany.

Figure 2. Prevalence of Polypharmacy by cancer type.



All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD; iqvia_belgium_lpd=IQVIA LPD Belgium; iqvia_germany_da=IQVIA DA Germany.

Figure 3 illustrates the distribution of frailty conditions by frailty category and solid cancer type (Breast, Colorectal, Endometrial, Lung, Ovarian, Pancreatic, and Prostate). For practically all cancer types and databases, the prevalence of frailty conditions among fit cancer patients was below 50% (except for hypertension in IQVIA LPD Belgium in endometrial and prostate cancer). The prevalence of conditions gradually shifted from left to right in the figure, representing an increasing prevalence of each condition by cancer type as the frailty category progressed in practically all databases (except for severe frailty in IQVIA LPD Belgium, where counts were too low to graph). Some conditions were over 90% for some cancer types in individuals with severe frailty, such as chronic kidney disease, hypertension, and visual impairment.

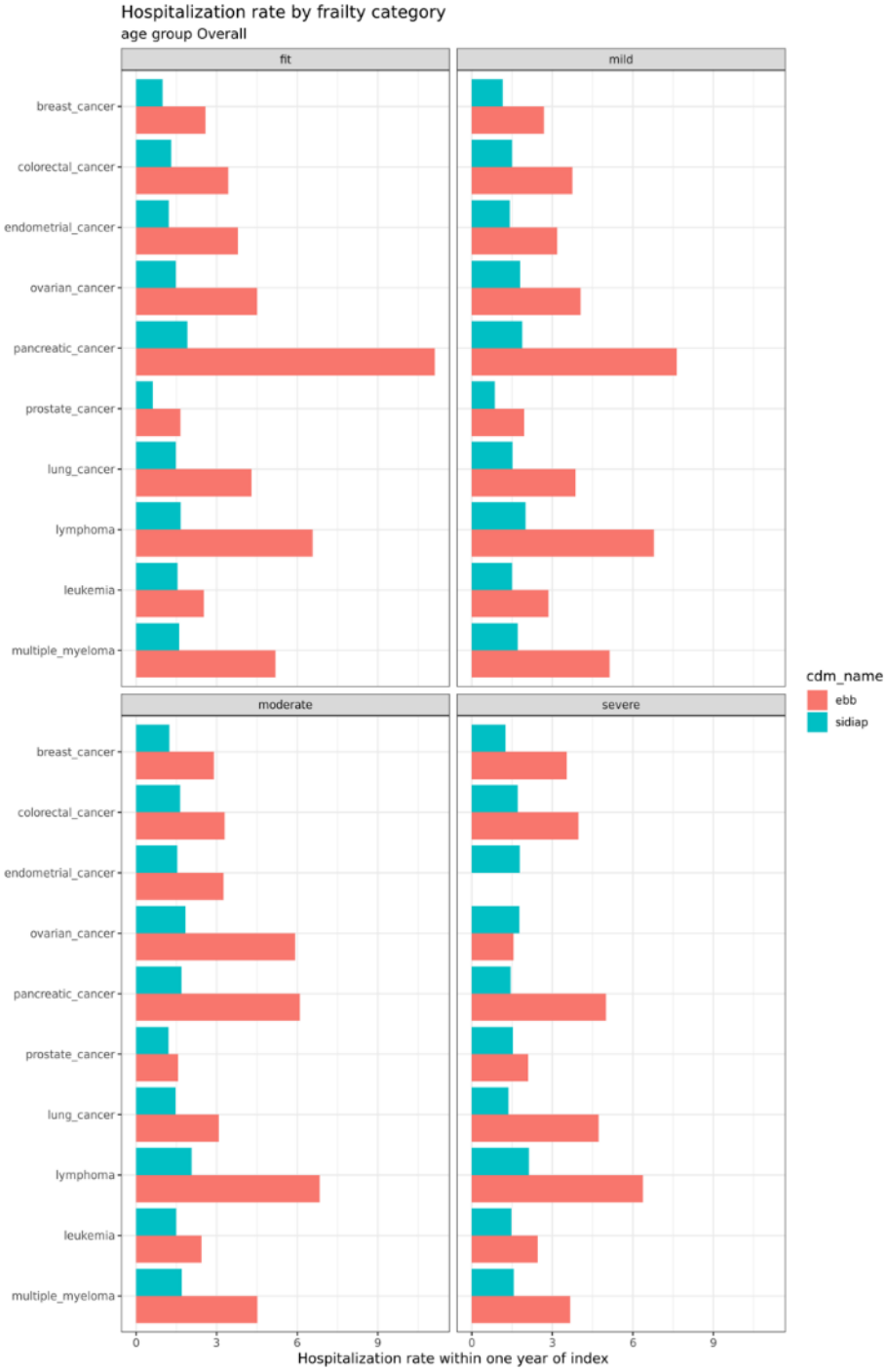
Figure 3. Prevalence of frailty conditions by frailty category and solid cancer type.

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD; iqvia_belgium_lpd=IQVIA LPD Belgium; iqvia_germany_da=IQVIA DA Germany.

One-year hospitalisation and mortality by cancer

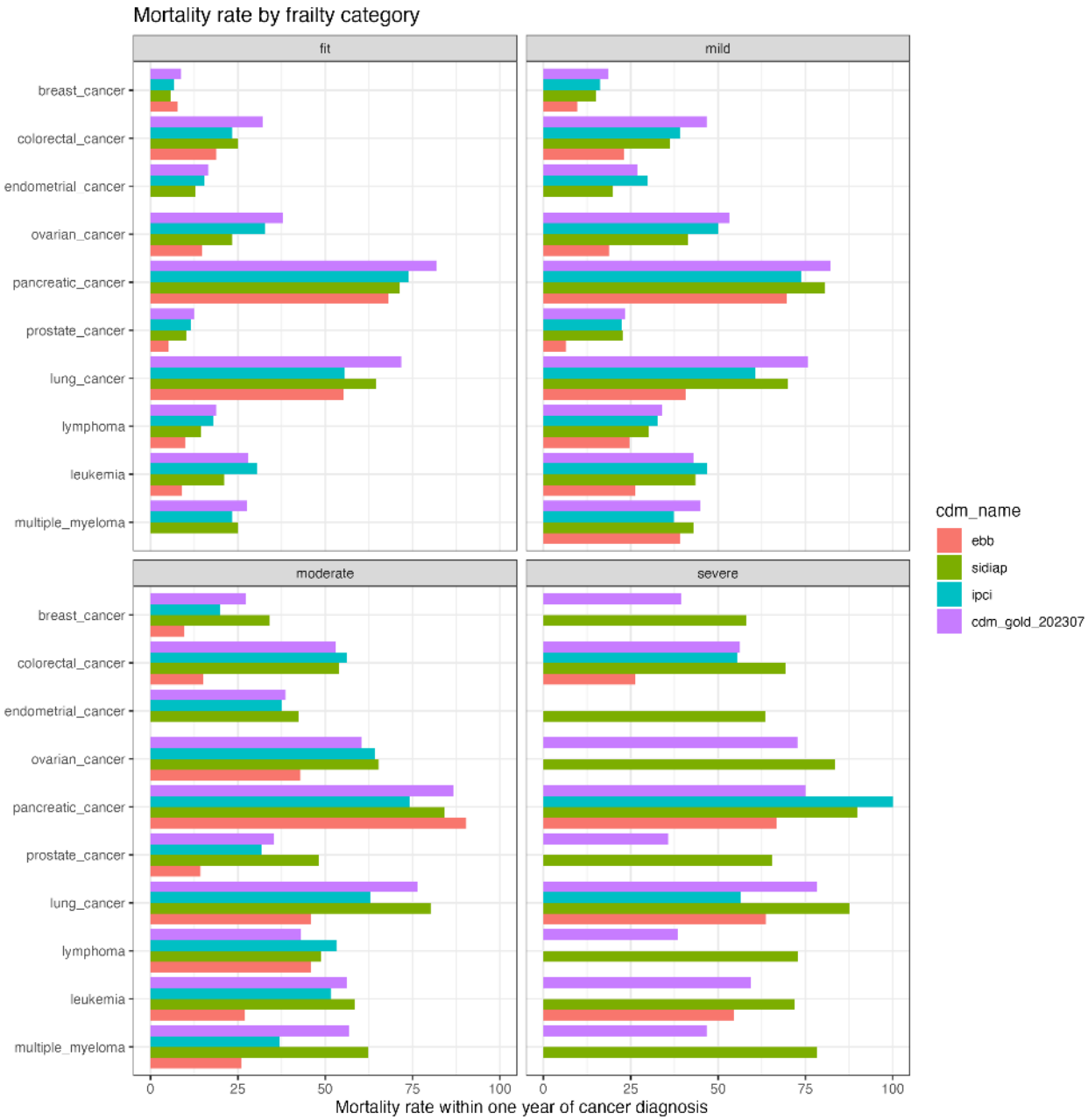
The one-year hospitalisation rate by frailty category for each cancer type is displayed in **I**
Figure 4. The one-year mortality risk by frailty category for each cancer type is shown in
Figure 5. The highest one-year hospitalisations rate was observed for pancreatic cancer in EBB. In SDIAP, no clear predominance was noted. For mortality risk, pancreatic cancer and lung cancer exhibited the highest mortality risks, irrespective of frailty severity. Other cancers seemed to display a positive gradient with increasing frailty. Results on mortality and hospitalisation by polypharmacy category by cancer type are available in the Shiny app (https://data-dev.darwin-eu.org/P2-C1-009-FrailtyPolypharmacyCancer/).

Figure 4. One-year hospitalisation rate by frailty category for each cancer type.



The hospitalisation rate was computed as the total number of hospitalisations within the year following the selected cancer diagnoses, divided by the total number of individuals within that category and period. A rate >1 indicates that the number of hospitalisations exceeded the number of individuals within that category. The mortality risk was computed as the total number of deaths within the year following the selected cancer diagnosis, divided by the total number of individuals within that category and period. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD.

Figure 5. One-year mortality risk by frailty category for each cancer type.



The hospitalisation rate was computed as the total number of hospitalisations within the year following the selected cancer diagnoses, divided by the total number of individuals within that category and period. A rate >1 indicates that the number of hospitalisations exceeded the number of individuals within that category. The mortality risk was computed as the total number of deaths within the year following the selected cancer diagnosis, divided by the total number of individuals within that category and period. Ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD.

12.6.4 Prevalence of Frailty and Polypharmacy by Cancer Type in Older Adults (aged >=65)

Among individuals aged 65 and above, the most prevalent cancer types were Breast, Colorectal, Prostate, and Lung cancer, like the overall population. However, the most prevalent cancer type varied by database. Within each database, the prevalence of each cancer type showed variations compared to the overall population. Among the most prevalent cancer types, the prevalence of breast cancer decreased, while it increased for Colorectal, Prostate, and Lung cancer. For the remaining cancer types, variations were more modest (**Appendix II. Table 20**).

In terms of median frailty score by cancer type in individuals 65 and above, the score generally increased with age for most cancer types and databases. The highest median frailty score observed was ovarian cancer in EBB among the 85 and above age group, followed by Leukaemia, at 0.31, also in EBB (**Appendix II. Table 21**).

The proportion of frailty categories (fit, mild, moderate, and severe) by cancer type varied with age. The highest prevalence of frailty by cancer type varied with age and database, and differences between cancer types were less marked compared to the overall population.

In the 65-74 age group, the proportion of fit individuals was approximately 50% or higher in almost all cancer types and databases (except EBB, in which it was lower). With increasing age, the proportion of fit individuals decreased in all databases and, in most cases, was below 50%. Conversely, the highest proportion of severely frail individuals was among the 85 and above age group and was highest in SIDIAP. In EBB and IQVIA LPD Belgium, not all cancer types had counts in the 85 and above age category (**Figure 6**).

Figure 6. Prevalence of frailty categories by cancer type in older adults (aged >=65).

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD; iqvia_belgium_lpd=IQVIA LPD Belgium; iqvia_germany_da=IQVIA DA Germany.

Polypharmacy, using the 5 thresholds, was highly prevalent among adults aged 65 and above. In the 65-74 age group, it was approximately 50% or above in almost all databases (except IQVIA Germany, where it was lowest). With increasing age, polypharmacy increased consistently among most cancer types in CPRD GOLD, IPCI, and SIDIAP, while the prevalence of polypharmacy in some cancer types varied slightly with age. Among the 85 and above group, no Polypharmacy 10 was observed in EBB, as well as for some cancer types in IQVIA LPD Belgium, while the prevalence of polypharmacy using both thresholds was lowest among all cancer types in IQVIA DA Germany (**Figure 7**).

Figure 7. Prevalence of Polypharmacy categories by cancer type in older adults (aged >=65).

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD; iqvia_belgium_lpd=IQVIA LPD Belgium; iqvia_germany_da=IQVIA DA Germany.

Figure 8, Figure 9, and **Figure 10** illustrate the distribution of frailty conditions by frailty category and solid cancer type (breast, colorectal, endometrial, lung, ovarian, pancreatic and prostate) in individuals aged 65-74, 75-84, and over 85. For practically all cancer types and databases, the prevalence of frailty conditions among fit cancer patients was below 50% in the 65-74 age group, while some conditions were over 50% in the 75-84 and 85 and above age groups. Similar to the overall population, the prevalence of conditions gradually shifted from left to right in the figure among all age groups, representing an increasing prevalence of each condition by cancer type as the frailty category progressed in practically all databases (except for severe frailty in IQVIA LPD Belgium, where counts were too low to graph). As observed in the overall

population, some conditions were over 90% for some cancer types in individuals with severe frailty in all 3 age groups, such as chronic kidney disease, hypertension, and visual impairment.

Figure 8. Prevalence of frailty conditions by frailty category and cancer type in older adults aged 65-74.

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD; iqvia_belgium_lpd=IQVIA LPD Belgium; iqvia_germany_da=IQVIA DA Germany.

Figure 9. Prevalence of frailty conditions by frailty category and cancer type in older adults aged 75-84.

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD; iqvia_belgium_lpd=IQVIA LPD Belgium; iqvia_germany_da=IQVIA DA Germany.

Figure 10. Prevalence of frailty conditions by frailty category and cancer type in older adults aged 85 and above.

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5. SIDIAP and EBB = databases with hospital/registry linkage. ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD; iqvia_belgium_lpd=IQVIA LPD Belgium; iqvia_germany_da=IQVIA DA Germany.

The Shiny app (https://data-dev.darwin-eu.org/P2-C1-009-FrailtyPolypharmacyCancer/) also contains a figure showing the distribution of frailty conditions by frailty category in blood cancers.

One-year hospitalisation and mortality by cancer in Older Adults (aged >=65)

The one-year hospitalisation rate by frailty category for each cancer type in older adults (aged >=65) is displayed in

Figure 4 The one-year mortality risk by frailty category for each cancer type in older adults (aged >=65) is shown in **Figure 12.** The highest one-year hospitalisations rate was observed for pancreatic cancer and lymphoma in EBB, which was highest in the 65-74 age group. In SDIAP, no clear predominance was noted, and hospitalisation decreased with age. For mortality risk, pancreatic cancer and lung cancer exhibited the highest mortality risks, irrespective of frailty severity and age. Ovarian cancer had very similarly high one-year mortality in the 85 and above age group. Within each frailty category and cancer type, mortality increased with age. There was no clear positive gradient with the increasing frailty category with each age category. Results on mortality and hospitalisation by polypharmacy category by cancer type are available in the Shiny app (https://data-dev.darwin-eu.org/P2-C1-009-FrailtyPolypharmacyCancer/).

Figure 11. One-year hospitalisation by cancer in Older Adults (aged >=65).

The hospitalisation rate was computed as the total number of hospitalisations within the year following the selected cancer diagnoses, divided by the total number of individuals within that category and period. A rate >1 indicates that the number of hospitalisations exceeded the number of individuals within that category. The mortality risk was computed as the total number of deaths within the year following the selected

cancer diagnosis, divided by the total number of individuals within that category and period. Ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD.

Figure 12. One-year mortality by cancer in Older Adults (aged >=65).

The hospitalisation rate was computed as the total number of hospitalisations within the year following the selected cancer diagnoses, divided by the total number of individuals within that category and period. A rate >1 indicates that the number of hospitalisations exceeded the number of individuals within that category. The mortality risk was computed as the total number of deaths within the year following the selected cancer diagnosis, divided by the total number of individuals within that category and period. Ebb=EBB; sidiap=SIDIAP; ipci=IPCI; cdm_gold_202307=CPRD GOLD.

13. MANAGEMENT AND REPORTING OF ADVERSE EVENTS/ADVERSE REACTIONS

In agreement with the Guideline on good pharmacovigilance practice (EMA/873138/2011), there will be no requirement for expedited reporting of adverse drug reactions as only secondary data will be used in this study.

14. DISCUSSION

14.1 Key Results

In this Key results section, we summarize all the main study findings. The next sections discuss limitations, interpretation of results, and generalisability.

We estimated the prevalence of frailty and polypharmacy among 350,203 individuals aged 18 and above (and 231,860, 66% were older adults, aged >=65), with an incident selected cancer diagnosis between 2017 and 2022, within the 6 participating databases (IQVIA DA Germany: 158,109; SIDIAP: 107,010; CPRD GOLD: 54,421; IPCI: 24,389; EBB: 3,310; IQVIA LPD Belgium: 2,964). The median age ranged between 65 (EBB) and 69 years (IPCI, CPRD GOLD, IQVIA DA Germany, and IQVIA LPD Belgium). Overall, the sex distribution among cancer patients was similar across all databases, with a slightly higher proportion of female cases among IPCI, CPRD GOLD, EBB, and IQVIA LPD Belgium. The median frailty score ranged between 0.056 (IPCI & IQVIA DA Germany) and 0.139 (EBB). The prevalence of frailty (including all individuals with mild to severe frailty) ranged between 23.7% (IQVIA DA Germany) and 58.3% (EBB). Among the individual frailty categories, most individuals included in this study were classified as fit, with a prevalence ranging across databases between 41.7% in EBB and 76.3% in IQVIA DA Germany. Across all databases, the proportion of individuals decreased with increasing frailty severity. The prevalence of severe frailty at incident-selected cancer diagnosis in these databases was low and ranged between 0.2% (IQVIA LPD Belgium) and 5.0% (EBB). The prevalence of polypharmacy using the >=5 threshold ranged between 19% (IQVIA DA Germany) and 56.2% (SIDIAP). The prevalence of polypharmacy decreased in all databases when the threshold increased to >=10 drugs, ranging from 4.3% (IQVIA DA Germany) to 22.9% in SIDIAP. The most prevalent condition identified (any time prior) within the study population was chronic kidney disease, and its prevalence increased with increasing frailty, reaching a prevalence of 90.1%-95.8% among those severely frail. One-year hospitalisation and mortality showed a positive gradient with increasing frailty severity. The one-year mortality among severely frail individuals was high, at 35-72%.

Frailty increased with age. Among older adults (aged >=65 and above), frailty (understood as mild, moderate, and severe categories combined) ranged between 22.6-70.2% among those aged 65-74, between 31.7-82.7% among those aged 75-84, and between 39.9-92.3% among those aged 85 and above. By frailty categories, mild frailty ranged between 17-42.7%, 20.7-41.7%, and. 26-41.3% in the 65-74, 75-84, and 85 and above age groups, respectively; moderate frailty ranged between 1.8-20.5%, 3.2-33%, and 7-41.5% in the 65-74, 75-84, and 85 and above age groups, respectively; and last, severe frailty ranged between 0.2-6%, 1.1-11.7%, and 2.2-19.1% in the 65-74, 75-84, and 85 and above age groups.

Polypharmacy (>=5 drugs threshold) increased with age. Among those aged 65-74, polypharmacy ranged between 19.4-62.6%, between 25-79.4% in those 75-84, and between 38-85.6% in those 85 and above

(among all databases, the lowest prevalence of polypharmacy was observed in IQVIA DA Germany, while the highest in SIDIAP).

Among older adults, one-year hospitalisation and mortality showed a positive gradient with increasing frailty severity and age. The one-year mortality among severely frail individuals was highest among those aged 85 and above, at 62-81%.

By individual cancer types, the highest prevalence of frailty was observed for pancreatic cancer, lung cancer, and multiple myeloma. These cancer types also showed the highest prevalence of polypharmacy in practically all databases.

Prevalence of frailty conditions

Some of the conditions included in the frailty score (without counting polypharmacy) returned zero counts. CPRD GOLD captured all conditions, followed by SIDIAP (only 1 condition with zero counts), while IPCI and IQVIA LPD Belgium were the databases with the highest number (6) of conditions with zero counts. The distribution of conditions varied by database, and some conditions showed marked differences in their prevalence across databases, such as fragility fracture, heart failure, and arthritis, among others. Among conditions reflecting disease state, foot problems returned zero counts in all databases, except CPRD GOLD. Among conditions reflecting symptoms and signs captured, falls also returned zero counts, except for CPRD GOLD, SIDIAP, and IQVIA LPD Belgium. Among conditions in the disability domain, housebound and requirement for care returned zero counts in more than one database (IPCI, EBB, IQVIA DA Germany, and IQVIA LPD Belgium for the former; and IPCI, EBB, and IQVIA LPD Belgium for the latter). Please see section 14.2 (Limitations of the Research Methods) for a full interpretation of differences between databases.

The 5 most prevalent conditions in each database were, in IPCI, chronic kidney disease (30.1%), hypertension (28.0%), urinary system disease (17.2%), visual impairment (15.7%), and respiratory disease (14.9%). For CPRD GOLD, chronic kidney disease (30.8%), hypertension (26.9%), Dyspnoea (21.7%), respiratory disease (21.3%), and dizziness (13.4%). For SIDIAP, chronic kidney disease (45.8%), hypertension (44.3%), visual impairment (32.7%), urinary system disease (27.0%), and anaemia (24.0%). For EBB, chronic kidney disease (56.7%), hypertension (53.5%), respiratory disease (43.6%), arthritis (37.1%), and visual impairment (36.4%). For IQVIA DA Germany, hypertension (40.5%), chronic kidney disease (32.3%), respiratory disease (21.7%), thyroid disease (18.5%), and diabetes (14.2%). For IQVIA LPD Belgium, hypertension (50.8%), respiratory disease (33.6%), sleep disturbance (31.2%), chronic kidney disease (23.5%), and diabetes (15.6%).

Characteristics of Individuals by Frailty Category

Overall, there was no clear sex predominance among individuals considered fit. Mild frailty displayed some variation in sex predominance by database, while for moderate and severe frailty, there was a clear predominance of female sex in all databases. The proportion of women increased with increasing frailty severity. Regarding age, the proportion of older individuals increased with increasing frailty scores also in all databases.

Regarding polypharmacy (using the =>5 drugs threshold), among fit, the prevalence of polypharmacy was inconsistent among databases and ranged between 6.6% (IQVIA DA Germany) and 39.8% (CPRD GOLD). Among frail, the prevalence of polypharmacy increased as frailty severity increased, and in severe frailty, polypharmacy was present in 89% and above. The prevalence of polypharmacy varied across databases. For example, mild frailty had a prevalence of polypharmacy between 45.7% in EBB and 86.9% in CPRD GOLD. However, for moderate frailty, the prevalence of polypharmacy was above 72% in all databases, and for severe frailty, it was consistently above 89%.

The prevalence of conditions included in the frailty score increased with increasing frailty severity category. Within the severe frailty category, some conditions reached a prevalence above 45% in all databases, such as chronic kidney disease (ranging between 90.1% in IPCI and 95.8% in EBB), hypertension (63.2% in CPRD GOLD to 96.3% in IQVIA DA Germany), and sleep disturbance (49% in SIDIAP to 85.5% in EBB) (Results on severe frailty in IQVIA LPD Belgium are not described because of low counts).

Characteristics of Individuals with Polypharmacy

Two thresholds of concomitant drug use were used to identify polypharmacy: >=5 and >=10 drugs. In terms of sex, there was a slight male predominance when the >=5 drugs threshold was used, while when using a >=10 drugs, there was a clear female predominance in some databases (IPCI, SIDIAP, EBB, and IQVIA LPD Belgium), while slight male predominance in the remaining (CPRD GOLD and IQVIA DA Germany). Regarding age, individuals with polypharmacy using the >=5 drugs threshold were generally within the 65-74 and 75-84 categories. Using the >=10 drugs polypharmacy threshold, most individuals were within the 75-84 and 85 and above category in almost all databases.

Within the >=5 drugs polypharmacy threshold, some conditions, such as chronic kidney disease, hypertension, and respiratory disease, had a prevalence of ~20% or above in all databases. Among the >=10 drugs polypharmacy category, the prevalence of conditions increased compared to >=5 drugs polypharmacy.

Prevalence Frailty and Polypharmacy by Period (pre- and post-2020)

Regarding age, EBB's median age increased from 64 to 66 in the post-2020 period, while the other databases varied slightly. The median frailty score remained unchanged in all databases, except for IPCI and EBB, which increased in the post-2020 period. However, there was a small increase in the proportion of patients within the mild, moderate, and severe frailty categories during the post-2020 period in all databases, except for CPRD GOLD and IQVIA DA Germany, which remained mostly unchanged. The prevalence of polypharmacy varied slightly.

The prevalence of the conditions in the frailty score varied slightly between periods. Some conditions displayed an increase by at least 5% in their prevalence in the post-2020 period and in at least one database: chronic kidney disease (5.5% in IQVIA LPD Belgium and 6.0% in SIDIAP) and fragility fracture (7.3% in EBB).

One-year mortality and hospitalisation by Frailty categories

Hospitalisation was available for EBB and SIDIAP and ranged, from fit to severely frail, between 1.18-1.54 in SIDIAP and 3.33-3.71 in EBB. SIDIAP had a clear positive gradient between hospitalisation rate and frailty and polypharmacy severity categories.

Mortality data was only available for IPCI, CPRD GOLD, SIDIAP, and EBB. All databases exhibited a positive gradient between mortality risk and the increasing severity of frailty and polypharmacy. The one-year mortality rate ranged between 13-25% among fit individuals and 35-72% among severely frail.

Large-scale characterisation by Polypharmacy and Frailty

The large-scale characterisation of conditions, procedures, signs, symptoms, and drugs in this report was based on a window of 365-31 days before the date of cancer diagnosis. Conditions related to hypertension, blood pressure findings, and heart disease were among the top 10 concepts in all databases. Respiratory system-related conditions, such as cough, dyspnoea, and chronic obstructive respiratory disease, were also among the top 10 concepts.

Influenza and SARS-COV-2 vaccination were among the 10 most common prescriptions in all databases, along with proton pump inhibitors, insulin sensitisers (metformin), blood pressure medications (calcium channel blockers, beta-blockers, diuretics), and analgesics (dipyrone and acetaminophen).

Characteristics of Frailty and Polypharmacy by Age, with a focus on older adults (aged >=65)

Stratification by age was focused on adults aged >=65.

In all databases, there was a male predominance between 65-84 years, after which, for most databases, a female predominance was observed (except for IQVIA LPD Belgium). The proportion of individuals with frailty increased with age. Frailty (understood as mild, moderate, and severe categories combined) ranged between 22.6-70.2% among those aged 65-74, between 31.7-82.7% among those aged 75-84, and between 39.9-92.3% among those aged 85 and above.

With increasing age, the proportion of individuals with greater frailty severity increased within each database. However, increments differed in each database. In this sense, in IPCI, for example, moderate frailty was 1.8% in the 65-74 age group and increased to 7.0% in the 85 and above age group, while in EBB, moderate frailty was 20.5% in the 65-74 age group and increased to 41.5% in the 85 and above age group. Similarly, severe frailty went 0.2% to 2.2 in IPCI, and 1.8 to 19.1 in SIDIAP, between the 65-74 and 85 and above age groups.

In terms of polypharmacy, using the >=5 drugs threshold, polypharmacy increased with age. Among those aged 65-74, polypharmacy ranged between 19.4-62.6%, between 25-79.4% in those 75-84, and between 38-85.6% in those 85 and above (among all databases, the lowest prevalence of polypharmacy was observed in IQVIA DA Germany, while the highest in SIDIAP).

One-year Hospitalisation Rate and Mortality Risk in Older Adults (aged >=65)

Regarding one-year hospitalisation, within each age group, hospitalisation increased with increasing severity of frailty and polypharmacy categories; however, within each frailty category, hospitalisation seemed to decrease with increasing age, in SIDIAP, while in EBB, there was no clear pattern.

In terms of one-year mortality, risks increased within each age group with increasing severity of frailty and polypharmacy categories. The same was observed within each frailty category with the increasing age.

Frailty and Polypharmacy by Sex

Across all databases, women had a lower median age than men. The median age for women ranged from 63 in EBB to 67 years in IPCI and CPRD GOLD. Among individual frailty categories, a slightly higher proportion of women was observed with increasing frailty severity. The prevalence of polypharmacy (>=5 threshold) was greater in men than women and ranged between 20.3% (IQVIA DA Germany) and 60.3% (SIDIAP) in men. However, the prevalence of polypharmacy using the >=10 threshold did not show a clear predominance by sex, except for IPCI, in which the prevalence was higher for men (16.3%) compared to women (13.0%).

The distribution of frailty conditions varied by sex: chronic kidney disease, fragility fracture, osteoporosis, and thyroid disease predominated in women, while cerebrovascular disease, hypertension, ischaemic heart disease, and peripheral vascular disease predominated in males.

The one-year hospitalisation rate was greater in males in SIDIAP, among the moderate and severe frailty categories, and polypharmacy (>=10 drugs). However, in EBB, the hospitalisation rate was higher among women for all categories compared to men, except for severe frailty, where it was greater for

women. One-year mortality was generally greater in men throughout all categories and databases (except for the severe frailty category in CPRD GOLD, in which mortality was higher in women).

Frailty and Polypharmacy by Cancer Type

Overall, the 4 most common cancer types in all databases were breast, colorectal, prostate, and lung cancer. Each cancer type showed distinct age and sex characteristics. Age-wise, among different cancer types and databases, individuals with breast cancer were generally younger, while multiple myeloma patients were generally older compared to other cancer types. In terms of median frailty score by cancer type, the cancers with the highest median frailty score were lung cancer (0.09-0.18), pancreatic cancer (0.09-0.18), and multiple myeloma (0.09-0.21).

The highest one-year hospitalisation rate was observed for pancreatic cancer in EBB. In SIDIAP, no clear predominance was noted. For mortality rate, pancreatic cancer and lung cancer exhibited the highest mortality rates, irrespective of frailty severity. Other cancers seemed to display a positive gradient with increasing frailty category.

Frailty and Polypharmacy by Cancer Type in older adults (aged >=65)

Like the overall population, the most prevalent cancer types among individuals aged 65 and above were Breast, Colorectal, Prostate, and Lung cancer. However, the most prevalent cancer type varied by database. Within each database, the prevalence of each cancer type showed variations compared to the overall population. Among the most prevalent cancer types, the prevalence of breast cancer decreased, while it increased for Colorectal, Prostate, and Lung cancer. For the remaining cancer types, variations were more modest.

In terms of median frailty score by cancer type in individuals 65 and above, the score generally increased with age for most cancer types and databases. The highest median frailty score observed was ovarian cancer in EBB among the 85 and above age group, followed by Leukaemia, at 0.31, also in EBB.

The proportion of frailty categories (fit, mild, moderate, and severe) by cancer type varied with age. The highest prevalence of frailty by cancer type varied with age and database, and differences between cancer types were less marked compared to the overall population.

In the 65-74 age group, the proportion of fit individuals was approximately 50% or higher in almost all cancer types and databases (except EBB, in which it was lower). With increasing age, the proportion of fit individuals decreased in all databases and, in most cases, was below 50%. Conversely, the highest proportion of severely frail individuals was among the 85 and above age group and was highest in SIDIAP. In EBB and IQVIA LPD Belgium, not all cancer types had counts in the 85 and above age category.

Polypharmacy, using the >= 5 drugs threshold, was highly prevalent among adults aged 65 and above. In the 65-74 age group, it was approximately 50% or above in almost all databases (except IQVIA Germany, where it was lowest). With increasing age, polypharmacy increased consistently among most cancer types in CPRD GOLD, IPCI, and SIDIAP, while the prevalence of polypharmacy in some cancer types varied slightly with age. Among the 85 and above group, no Polypharmacy (>=10 drugs) was observed in EBB, as well as for some cancer types in IQVIA LPD Belgium, while the prevalence of polypharmacy using both >= 5 and >=10 thresholds was lowest among all cancer types in IQVIA DA Germany.

In terms of the distribution of frailty conditions by frailty category and solid cancer type (breast, colorectal, endometrial, lung, ovarian, pancreatic and prostate) in individuals aged 65-74, 75-84, and over 85, for practically all cancer types and databases, the prevalence of frailty conditions among fit cancer patients was below 50% in the 65-74 age group, while some conditions were over 50% in the 75-84 and 85 and above age groups. Similar to the overall population, the prevalence of conditions gradually increased their proportion, as frailty increased, with increasing age, representing an increasing prevalence of each

condition by cancer type as the frailty category progressed in practically all databases (except for severe frailty in IQVIA LPD Belgium, where counts were too low to graph). As observed in the overall population, some conditions were over 90% for some cancer types in individuals with severe frailty in all 3 age groups, such as chronic kidney disease, hypertension, and visual impairment.

One-year hospitalisation and mortality by cancer Type in Older Adults (aged >=65)
The highest one-year hospitalisation rate in older adults (aged >=65) was observed for pancreatic cancer and lymphoma in EBB, which was highest in the 65-74 age group. In SIDIAP, no clear predominance was noted, and hospitalisation decreased with age. Regarding mortality risk in older adults (aged >=65), pancreatic cancer and lung cancer exhibited the highest mortality risks, irrespective of frailty severity and age. Ovarian cancer had very similarly high one-year mortality in the 85 and above age group. Within each frailty category and cancer type, mortality increased with age. There was no clear positive gradient with the increasing frailty category with each age category.

14.2 Limitations of the Research Methods

The study was informed by routinely collected healthcare data, so data quality issues must be considered. In particular, the identification of cancer patients is likely to vary across databases. While we expected relatively few false positives, false negatives may be more likely, especially for databases without patient-level linkage to secondary care data. In these databases, information from hospitalisations and outpatient services are usually required to be sent to the general practitioners' office; therefore, general practitioners would be aware of malignant cancer diagnoses. However, this may not always be done because it may entail coding the episode (diagnoses, treatments, and prescriptions received in hospital or specialist clinics into the electronic record so they can be used in research). Regarding false positives, some databases included in this study have mapped cancer diagnosis from ICD-10; because ICD-10 does not adequately reflect topography and morphology for some cancer diagnoses, this could lead to the inclusion of false positives for the selected cancer. Specifically, cases were mapped under high-upstream concepts for some cancer sites and databases, which could lead to misclassification. Overall, the issues stated above may have implications for the prevalence of certain cancers and may affect the precision of results, under or overestimating them. Nevertheless, cancer diagnosis has been previously validated in the SIDIAP and CPRD databases (24, 63, 64), and the EEB database is linked to cancer registry data, which is known to contain high-quality data on cancer diagnoses.

Additionally, phenotyping for cancer and frailty is complex. Phenotyping was based on previous literature, in addition to several review rounds, and CohortDiagnostics runs. However, given that the project's purpose was to undergo a conservative assessment of frailty prevalence within the 10 selected cancer types, it must be noted that the concept codes used to identify each selected cancer and condition within frailty may, in some cases, be incomplete, inaccurate, or both, because the rigorous and complex phenotyping procedures could not always be fully applied to the high number of descendent codes needed for this study.

The recording of hospitalisation and date of death varied across databases. Therefore, one-year hospitalisation rates and mortality risks were not calculated in all databases. In this sense, hospitalisation rates are reliably recorded in SIDIAP and EBB due to data linkage. Mortality could not be calculated in IQVIA DA Germany and IQVIA LPD Belgium because the date of death is not systematically recorded.

Polypharmacy was defined as the use of concomitant medications using primarily community prescribing. For the polypharmacy definition, we identified medication use by counting the maximum number of drugs by ingredient level prescribed on any given day within a time window before the index date. We did not consider the use of more than one drug from the same class in the count as patients may have switched

during this time period rather than receive concomitant use. We also cannot be certain that all use is concomitant during this time period, with the risk of misclassification being greater as look back time periods increase. A 90-day window was considered reasonable based on the experience of repeat drug prescribing typically occurring in primary care. Polypharmacy estimates differed across databases. The underlying reasons are likely complex. Notably, of the 3 databases with lower estimates, two (IQVIA DA Germany and IQVIA LPD) are exclusively GP-record-based, with no hospital linkage. However, it is unlikely that regular hospital-prescribed drugs could account for differences with other databases. Estimates for IQVIA DA Germany are in line with previous estimates (65). With regards to lower prevalence of polypharmacy in EBB, since polypharmacy increases with age, this could be related to the lower participation of older adults in this cohort (30).

Finally, it is important to note that while the frailty score calculated in this study was based on frequently used conditions included in validated frailty indexes (3, 33), we only used the proposed conditions for defining the score, and no validation of its performance or discrimination was done. These indexes were not developed specifically for cancer patients but rather to assess frailty at the population level and within specific healthcare systems and their EHRs. This could have led to an underestimation of frailty in our population and misclassification in several ways, such as potential differences between relevant deficit-based conditions in cancer patients compared to the general population, inadequate data collection, and phenotyping In this sense, some included conditions were not always identified across all databases, leading to zero counts for certain conditions (3, 33). Moreover, some conditions in the frailty score may likely remain unrecorded using diagnostic codes in databases, especially among those entailing more subjective valuations, such as social vulnerability or requirement for care. Variables related to certain deficits, like foot problems and social vulnerabilities, are often poorly recorded, contributing to potential underestimation. Regardless, we also observed that some disabilities and symptoms, such as visual and hearing impairments, sleep disturbances, or cognitive problems, gained relevance as frailty increased. Further work on phenotyping may lead to improvements related to identifying other disabilities and signs and symptoms. Despite these limitations, we identified a gradient between frailty categories and outcomes, such as hospitalisation and mortality, which were consistent with those observed in studies using other scores. Additionally, our results suggest that the gradient observed between frailty severity and outcomes was not entirely dependent on medical conditions, in which adverse outcomes would be more expected.
In summary, a key objective of this study was to assess the applicability of this approach, and these findings suggest that even with the current limitations, the frailty score may provide meaningful insights..

14.3 Interpretation

Frailty is a multidimensional syndrome reflecting the degree of an individual's functional reserve to acute endogenous or exogenous stressors and has been recognised as a key barrier to successful cancer treatments, especially among older adults (66). Hence the European Society for Medical Oncology, the International Society of Geriatric Oncology, the National Comprehensive Cancer Network, and the American Society of Clinical Oncology recommend a geriatric assessment to optimise decision-making in older patients with cancer (67-70). However, significant barriers to implementing geriatric assessments uniformly have been noted, related to time, support, and referral options, and mostly rely on providers' judgment and are limited to certain domains (such as functional status and falls) (71). In this sense, using an automated approach by using EHR-based frailty scores offers the possibility of adopting these measures on a large scale, which can prove useful in optimal decision-making regarding cancer patient care.

In the general population, the prevalence of frailty among those aged 65 and over is estimated at ~10% and ranges between 25 and 50% among those aged 85 and above. Among older adults with cancer, a

systematic review assessing the prevalence of frailty among individuals with different cancer types and a median age of 70, estimated a prevalence of 42% (range 6%–86%), while pre-frailty (1-2 conditions) at 43% (range 13%–79%). Our study assessed frailty using routinely gathered EHR data on 35 conditions, disabilities, signs and symptoms, in addition to polypharmacy, as proposed in prior EHR indexes (3, 33). Within our study, which included individuals above 18 years and a median age of 65-69 years, the prevalence of frailty (including all individuals with mild to severe frailty) ranged between 23.7% (IQVIA DA Germany) and 58.3% (EBB). While pre-frailty was not assessed, pre-frailty (understood as the presence of 1-2 conditions) is likely represented within the fit population, which ranged between 41.7-76.3%. In our study, we observed that frailty increased with age. Frailty (including all individuals with mild to severe frailty) among those aged >=65, ranged between 22.6-70.2% among those aged 65-74, between 31.7-82.7% among those aged 75-84, and between 39.9-92.3% among those aged 85 and above, which is consistent with prior studies (12).

Older people with frailty and pre-frailty are at increased risk of all-cause mortality, postoperative mortality, chemotherapy intolerance and postoperative complications and may also be at increased risk of chemotherapy-related side effects. In this sense, we observed a positive gradient between hospitalisation and frailty severity, which ranged from fit to frail by database, from 1.18-1.54% in SIDIAP to 3.33-3.71% in EBB. The fact that one-year hospitalisation rates were >1 indicates the occurrence of readmissions. A positive gradient was also observed between one-year mortality risk and frailty severity and polypharmacy. The one-year mortality risk ranged between 13% and 25% among fit individuals and reached 35-72% among severely frail individuals. Mortality increased with age, and the one-year mortality among severely frail individuals was highest among those aged 85 and above, at 62-81%. In this line, other studies have described a positive gradient between increasing Clinical Frailty Scores and higher readmission rates, longer hospital stays, postoperative mortality, and morbidity (72). Additionally, the gradients observed between the frailty categories and the outcomes we observed were consistent with the performance of the electronic frailty indexes on which it was based (3, 33). Furthermore, we observed that with increasing frailty scores, the prevalence of disabilities and signs and symptoms also increased, underlining that the accumulation of deficits was not exclusively reliant on conditions. This observation highlights the score's ability to capture multiple frailty deficits effectively. It would be interesting to further understand to what extent the different types of deficits (conditions, disabilities, and signs and symptoms) contribute to the adverse outcomes observed. Exploring this relationship could provide deeper insights into the mechanisms of frailty and help tailor more effective interventions for mitigating risks associated with frailty.

Regarding the prevalence of conditions included in the frailty score, chronic kidney disease was the most prevalent in the study population, ranging between 30.1 and 56.7% across data sources. The prevalence of chronic kidney disease increased with increasing frailty and reached a prevalence of 86.6-95.7% among those severely frail. Some studies have estimated the prevalence of chronic kidney disease among cancer patients between 12 and 53% at cancer diagnosis (73, 74). Additionally, cancer patients with concomitant chronic kidney disease have worse cancer outcomes compared to those with normal kidney function (75). Despite the high prevalence of kidney dysfunction and its prognostic implications, there is limited evidence to guide cancer treatment in patients with chronic kidney disease. The high prevalence of chronic kidney disease among frail individuals with cancer observed within our study may be relevant because this could have implications regarding polypharmacy, given many medications can accentuate chronic kidney disease, and polypharmacy has been associated with elevated risks of all-cause and cardiovascular disease mortality among elderly chronic kidney disease patients in the general population (76). Within the overall patient population, polypharmacy ranged between 19.0 and 56.2%, and in those 75 and above, it ranged between 25-85.6%. However, polypharmacy was approximately 50% or above in all databases among all individuals considered to be frail, while it was consistently above 75% among moderate and severely frail patients.

14.4 Generalisability

This study included data from 6 databases from 6 different European countries/regions (Estonia, Germany, The Netherlands, Spain (Catalonia), Belgium, and the United Kingdom) and healthcare systems (primary care in SIDIAP, IQVIA Germany, IQVIA LPD Belgium, IPCI, and CPRD GOLD, and biobank in EBB). However, we may have underestimated the prevalence of frailty in some data sources, as we were not always able to identify all concept sets used to define frailty conditions. Additionally, some data sources could not inform on date of death. In this line, hospitalisation could only be informed in SIDIAP and EBB. Thus, these results are only representative of the Catalonian and Estonian populations.

While these results may be considered largely representative of individuals, especially older people, newly diagnosed with cancer in the respective countries/regions, results should not be generalised to Europe as differences in population characteristics and how patients may be diagnosed with cancer may vary by country. Frailty and polypharmacy results must be interpreted with caution, mainly for two reasons. First, while the frailty score used to identify the prevalence of frailty was based on conditions included among previously validated EHR frailty indexes, the phenotype we used is likely conservative in categorising people into frailty categories and could benefit from further development and validation. Second, the performance of these scores can vary depending on databases and data quality, as not all databases record relevant information, and mapping of some of the conditions of interest may vary across sources. Likewise, the frailty score used in this study is a stratification tool that identifies individuals at risk of different degrees of frailty. Hence, this score is not intended as a diagnostic tool for which validated scales are available and is only intended to describe the magnitude of frailty within the specific population.

Despite the estimates being conservative, frailty seems identifiable with our approach. Furthermore, the gradient we identified between frailty categories and outcomes (hospitalisation and mortality) is consistent with prior studies. However, further work is required to optimise the score and confirm its validity.

15. CONCLUSION

We estimated the prevalence of frailty and polypharmacy among 350,203 individuals aged 18 and above (amongst which 66% were older adults aged 65 years or more) with incident-selected cancer types diagnosed between 2017 and 2022 within the 6 participating databases/countries. The prevalence of frailty (including all individuals with mild to severe frailty) ranged between 23.7% (IQVIA DA Germany) and 58.3% (EBB), and increased with age. Among those aged >=65, frailty ranged between 22.6-70.2% in the 65-74 group, 31.7-82.7% in the 75-84 group, and between 39.9-92.3% in the 85 and above group. The prevalence of polypharmacy (using the >=5 drugs threshold) ranged between 19.0-56.2% in the overall population and increased to 19.4-62.6% in the 65-74 age group, 25-79.4% in the 75-84 age group, and 38-85.6% in the 85 and above age group. One-year hospitalisation and mortality showed a positive gradient with increasing frailty severity. The one-year mortality among severely frail individuals ranged from 35%-72% and increased to 62-81% among those aged 85 and above. The most prevalent condition identified within the study population was chronic kidney disease, and its prevalence increased with increasing frailty, reaching a prevalence of 90% among those severely frail.

Our estimates underscore a high prevalence of frailty among cancer patients, which is at least doubled that of the general population (estimated at 10% in individuals 65 and above). Additionally, our results are consistent with prior frailty estimates among cancer patients. Furthermore, the gradient observed between the frailty categories and the hospitalisation and mortality outcomes is compatible with the performance of the electronic frailty indexes on which our score was based and similar to what has been described with Clinical Frailty Scores, which reassures that frailty seems identifiable by our approach. Still, our results

displayed some heterogeneity across databases, most likely related to data capture, suggesting that frailty scores from some sources may be conservative. Regardless, frailty index scores have the potential to be measured in some RWD datasets, and this approach could potentially be applicable to medicine evaluations or other areas if needed. While further work to optimise phenotype and assess its performance in other databases may be needed for optimal applicability, these findings suggest that despite the current limitations, the frailty score we implemented may provide meaningful insights.

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17. ANNEXES

Appendix I: List of Stand-Alone documents

Appendix II: Supplementary Tables

Appendix I.

Appendix I. Table 1. Concept sets used to identify the selected cancer types.

Cancer	concept_id	concept_name
Lung; https://atlas-demo.ohdsi.org/#/cohortdefinition/1788638/conceptsets/	3654352	Anaplastic lymphoma kinase fusion oncogene positive non-small cell lung cancer
	3654297	Anaplastic lymphoma kinase fusion oncogene negative non-small cell lung cancer
	4110705	Squamous cell carcinoma of lung
	3654301	Reactive oxygen species 1 negative non-small cell lung cancer
	4115276	Non-small cell lung cancer
	4140471	Epidermal growth factor receptor negative non-small cell lung cancer
	4143825	Epidermal growth factor receptor positive non-small cell lung cancer
	36716426	Reactive oxygen species 1 positive non-small cell lung cancer
	37109576	Squamous non-small cell lung cancer
	45766129	Non-small cell lung cancer with mutation in epidermal growth factor receptor
	45766131	Non-small cell lung cancer without mutation in epidermal growth factor receptor
	602150	Primary adenocarcinoma of middle lobe of right lung
	602159	Primary small cell carcinoma of lower lobe of left lung
	602161	Primary small cell carcinoma of upper lobe of left lung
	602163	Primary squamous cell carcinoma of upper lobe of left lung
	602167	Primary squamous cell carcinoma of lower lobe of right lung
	602169	Primary squamous cell carcinoma of middle lobe of right lung
	602171	Primary squamous cell carcinoma of upper lobe of right lung
	602696	Primary small cell carcinoma of upper lobe of right lung
	602697	Primary squamous cell carcinoma of lower lobe of left lung
	602682	Primary large cell carcinoma of lower lobe of right lung
	602695	Primary small cell carcinoma of middle lobe of right lung
	605476	Primary small cell carcinoma of lower lobe of right lung
	605821	Non-small cell lung carcinoma with NRG1 fusion
	608925	Primary small cell carcinoma of right lung
	608926	Primary small cell carcinoma of left lung
	609075	Primary non-small cell carcinoma of lower lobe of left lung
	609076	Primary non-small cell carcinoma of middle lobe of right lung
	609077	Primary non-small cell carcinoma of upper lobe of left lung

	609078	Primary non-small cell carcinoma of lower lobe of right lung
	609079	Primary non-small cell carcinoma of right lung
	609080	Primary non-small cell carcinoma of left lung
	609081	Primary non-small cell carcinoma of upper lobe of right lung
	605445	Primary large cell carcinoma of lower lobe of left lung
	605446	Primary large cell carcinoma of upper lobe of left lung
	605447	Primary large cell carcinoma of upper lobe of right lung
	4110589	Large cell carcinoma of lung
	4110590	Giant cell carcinoma of lung
	4110591	Small cell carcinoma of lung
	4110705	Squamous cell carcinoma of lung
	4112738	Adenocarcinoma of lung
	4112739	Oat cell carcinoma of lung
	4155293	Carcinoma of lower lobe, bronchus or lung
	4308784	Adenocarcinoma of lung, stage I
	4312274	Squamous cell carcinoma of lung, TNM stage 4
	4314040	Large cell carcinoma of lung, TNM stage 1
	4314156	Adenocarcinoma of lung, stage IV
	4314172	Non-small cell carcinoma of lung, TNM stage 2
	4314832	Adenocarcinoma of lung, stage II
	4307118	Large cell carcinoma of lung, TNM stage 2
	4308479	Non-small cell carcinoma of lung, TNM stage 4
	4310703	Non-small cell carcinoma of lung, TNM stage 1
	4311452	Adenocarcinoma of lung, stage III
	4311997	Non-small cell carcinoma of lung, TNM stage 3
	4312768	Large cell carcinoma of lung, TNM stage 3
	4310448	Squamous cell carcinoma of lung, TNM stage 1
	4313200	Squamous cell carcinoma of lung, TNM stage 2
	4313751	Large cell carcinoma of lung, TNM stage 4
	4322387	Squamous cell carcinoma of lung, TNM stage 3
	36686537	Large cell carcinoma of left lung
	36686538	Large cell carcinoma of right lung
	36712815	Squamous cell carcinoma of left lung
	36712816	Squamous cell carcinoma of right lung
	36712981	Adenocarcinoma of right lung
	36717017	Primary adenocarcinoma of upper lobe of right lung
	36712707	Primary adenocarcinoma of lower lobe of left lung
	36712708	Primary adenocarcinoma of upper lobe of left lung
	36712709	Primary adenocarcinoma of lower lobe of right lung
	36713366	Extensive stage primary small cell carcinoma of lung
	37311684	Acinar cell cystadenocarcinoma of lung
	40492938	Carcinoma of lung

	42539251	Adenocarcinoma of left lung
	45768916	Primary adenocarcinoma of lung
	45768917	Primary mucinous adenocarcinoma of lung
	45768918	Primary clear cell squamous cell carcinoma of lung
	45768919	Primary basaloid squamous cell carcinoma of lung
	45768920	Primary undifferentiated carcinoma of lung
	45768921	Primary spindle cell carcinoma of lung
	45768922	Primary pleomorphic carcinoma of lung
	45768923	Primary pseudosarcomatous carcinoma of lung
	45768927	Primary myoepithelial carcinoma of lung
	45768928	Primary adenoid cystic carcinoma of lung
	45768929	Primary salivary gland type carcinoma of lung
	45768930	Primary mixed mucinous and non-mucinous bronchiolo-alveolar carcinoma of lung
	45768931	Primary non-mucinous bronchiolo-alveolar carcinoma of lung
	45768932	Primary mucinous bronchiolo-alveolar carcinoma of lung
	45769034	Primary mucinous cystadenocarcinoma of lung
	45768879	Primary fetal adenocarcinoma of lung
	45768880	Primary mixed subtype adenocarcinoma of lung
	45768881	Primary adenosquamous carcinoma of lung
	45768883	Primary small cell non-keratinizing squamous cell carcinoma of lung
	45768884	Primary acinar cell carcinoma of lung
	45768885	Primary solid carcinoma of lung
	45768886	Primary papillary adenocarcinoma of lung
	45772933	Primary signet ring cell carcinoma of lung
	45772938	Primary papillary squamous cell carcinoma of lung
	45772939	Primary mucoepidermoid carcinoma of lung
	46272955	Primary clear cell adenocarcinoma of lung
	4111804	Squamous cell carcinoma of trachea
	4112736	Adenoid cystic carcinoma of trachea
	45768933	Primary clear cell adenocarcinoma of trachea
	45768934	Primary papillary adenocarcinoma of trachea
	45768935	Primary mucinous adenocarcinoma of trachea
	45768936	Primary adenocarcinoma of trachea
	45768855	Primary signet ring cell carcinoma of trachea
	45768856	Primary myoepithelial carcinoma of trachea
	45768857	Primary mucoepidermoid carcinoma of trachea
	45768858	Primary salivary gland type carcinoma of trachea
	45768860	Primary mucinous cystadenocarcinoma of trachea
	45768861	Primary solid carcinoma of trachea
	45768862	Primary undifferentiated carcinoma of trachea
	45768863	Primary acinar cell carcinoma of trachea
	45768865	Primary squamous cell carcinoma of trachea

	45768866	Primary clear cell squamous cell carcinoma of trachea
	45768867	Primary papillary squamous cell carcinoma of trachea
	45768868	Primary giant cell carcinoma of trachea
	45768869	Primary adenosquamous carcinoma of trachea
	45768870	Primary spindle cell carcinoma of trachea
	45768952	Primary lymphoepithelial carcinoma of trachea
	45768953	Primary squamous cell adenoid carcinoma of trachea
	45772932	Primary basaloid squamous cell carcinoma of trachea
	45772942	Primary verrucous carcinoma of trachea
	4177112	Malignant tumor of trachea
	4241676	T4: Lung tumor of any size that invades any of the following: mediastinum; heart; great vessels; trachea; esophagus; vertebral body; carina
	258369	Primary malignant neoplasm of lung
	443388	Malignant tumor of lung
	619299	Primary malignant neoplasm of left lung
	619300	Primary malignant neoplasm of right lung
	4293156	pT2: Tumor of lung as per AJCC 6th Edition definition (lung)
	4298502	pT4: Tumor of lung as per AJCC 6th Edition definition (lung)
	45769098	Primary malignant epithelial neoplasm of trachea
	443399	Malignant tumour of bronchus
	4208307	Nonsquamous nonsmall cell neoplasm of lung
	4197581	Squamous cell carcinoma of bronchus in left upper lobe
	4196725	Squamous cell carcinoma of bronchus in right lower lobe
	4197582	Squamous cell carcinoma of bronchus in right middle lobe
	4197583	Squamous cell carcinoma of bronchus in right upper lobe
	4196724	Squamous cell carcinoma of bronchus in left lower lobe
	37395650	Primary small cell malignant neoplasm of lung, TNM stage 3
	37395648	Primary small cell malignant neoplasm of lung, TNM stage 1
	37395649	Primary small cell malignant neoplasm of lung, TNM stage 2
	37395651	Primary small cell malignant neoplasm of lung, TNM stage 4
	4094874	Malignant neoplasm of cartilage of trachea
	4247821	Primary malignant neoplasm of carina
	4092215	Malignant neoplasm of carina of bronchus
	4095449	Malignant neoplasm of mucosa of trachea
	432262	Primary malignant neoplasm of trachea
	433973	Primary malignant neoplasm of bronchus of left lower lobe
	4246121	Primary malignant neoplasm of hilus of lung
	4246804	Primary malignant neoplasm of bronchus of right middle lobe
	4247832	Primary malignant neoplasm of lower lobe of left lung
	45769035	Primary carcinosarcoma of lung
	45769097	Pleuropulmonary blastoma type III
	4312567	Primary malignant neoplasm of upper lobe of right lung

	45769095	Pleuropulmonary blastoma type I
	36716500	Primary malignant neuroendocrine neoplasm of lung
	4157454	Primary malignant neoplasm of lower lobe, bronchus or lung
	619301	Bilateral primary malignant neoplasm of lungs
	4246027	Primary malignant neoplasm of bronchus of left upper lobe
	4246148	Primary malignant neoplasm of right lower lobe of lung
	45769096	Pleuropulmonary blastoma type II
	45769094	Pleuropulmonary blastoma
	4110706	Pancoast tumor
	4311501	Primary malignant neoplasm of right middle lobe of lung
	40391740	Pulmonary blastoma
	4247727	Primary malignant neoplasm of bronchus of right lower lobe
	258375	Overlapping malignant neoplasm of bronchus and lung
	4246805	Primary malignant neoplasm of bronchus of right upper lobe
	4246126	Primary malignant neoplasm of left upper lobe of lung
	4111807	Epithelioid hemangioendothelioma of lung
	4151250	Malignant neoplasm of upper lobe, bronchus or lung
	4089756	Malignant neoplasm of lower lobe of lung
	37110034	Malignant neoplasm of right upper lobe of lung
	37110032	Malignant neoplasm of upper lobe of left lung
	37110033	Malignant neoplasm of lower lobe of left lung
	4092216	Malignant neoplasm of upper lobe of lung
	765056	Malignant carcinoid tumor of lung
	4110587	Malignant tumor of lung parenchyma
	37110031	Malignant neoplasm of lower lobe of right lung
	4092218	Malignant neoplasm of middle lobe bronchus
	4089754	Malignant neoplasm of middle lobe of lung
	602698	Primary squamous cell carcinoma of left main bronchus
	37111619	Malignant carcinoid tumor of bronchus
	257503	Primary malignant neoplasm of main bronchus
	4089755	Malignant neoplasm of lower lobe bronchus
	4162250	Carcinoma of main bronchus
	37116436	Malignant epithelial neoplasm of bronchus
	602160	Primary small cell carcinoma of left main bronchus
	602168	Primary squamous cell carcinoma of right main bronchus
	605477	Primary small cell carcinoma of right main bronchus
	4157333	Malignant neoplasm of main bronchus
	442139	Primary malignant neoplasm of bronchus
	36716499	Primary malignant neuroendocrine neoplasm of bronchus
	4111805	Squamous cell carcinoma of bronchus
	601155	Primary malignant neoplasm of right main bronchus
	4095450	Malignant neoplasm of upper lobe bronchus

	605430	Primary adenocarcinoma of left main bronchus
	601154	Primary malignant neoplasm of left main bronchus
	602149	Primary adenocarcinoma of right main bronchus
	258369	Primary malignant neoplasm of lung
	443388	Malignant tumor of lung
	443399	Malignant tumor of bronchus
	619299	Primary malignant neoplasm of left lung
	619300	Primary malignant neoplasm of right lung
	3181040	Metastatic lung carcinoma
	4110587	Malignant tumor of lung parenchyma
	4177112	Malignant tumor of trachea
	4196724	Squamous cell carcinoma of bronchus in left lower lobe
	4196725	Squamous cell carcinoma of bronchus in right lower lobe
	4197581	Squamous cell carcinoma of bronchus in left upper lobe
	4197582	Squamous cell carcinoma of bronchus in right middle lobe
	4197583	Squamous cell carcinoma of bronchus in right upper lobe
	4241676	T4: Lung tumor of any size that invades any of the following: mediastinum; heart; great vessels; trachea; esophagus; vertebral body; carina
	4293156	pT2: Tumor of lung as per AJCC 6th Edition definition (lung)
	4298502	pT4: Tumor of lung as per AJCC 6th Edition definition (lung)
	4311499	Primary malignant neoplasm of respiratory tract
	4334322	Malignant neoplasm of lower respiratory tract
	35610164	Malignant neoplasm of respiratory tract
	36520546	Lymphoepithelial carcinoma of overlapping lesion of lung
	36525571	Squamous cell carcinoma, adenoid of upper lobe, lung
	36526753	Metaplastic carcinoma, NOS, of lung, NOS
	36529691	Giant cell and spindle cell carcinoma of upper lobe, lung
	36531120	Adenoid cystic carcinoma of overlapping lesion of lung
	36531819	Squamous cell carcinoma, NOS, of overlapping lesion of lung
	36533028	Malignant tumor, small cell type of lung, NOS
	36533051	Lymphoepithelial carcinoma of lung, NOS
	36535903	Squamous cell carcinoma, spindle cell of overlapping lesion of lung
	36538987	Verrucous carcinoma, NOS, of lower lobe, lung
	36545242	Adenoid cystic carcinoma of upper lobe, lung
	36548201	Squamous cell carcinoma, adenoid of middle lobe, lung
	36549159	Squamous cell carcinoma, microinvasive of middle lobe, lung
	36550205	Carcinosarcoma, NOS, of overlapping lesion of lung
	36552316	Small cell carcinoma, fusiform cell of upper lobe, lung
	36553640	Carcinosarcoma, NOS, of middle lobe, lung
	36557444	Desmoplastic small round cell tumor of lung, NOS
	36684857	Metastatic non-small cell lung cancer
	36716500	Primary malignant neuroendocrine neoplasm of lung

	40493428	Malignant neoplasm of respiratory system
	44499010	Squamous cell carcinoma, NOS, of middle lobe, lung
	44499488	Squamous cell carcinoma, NOS, of lower lobe, lung
	44499625	Small cell carcinoma, intermediate cell of upper lobe, lung
	44499626	Combined small cell carcinoma of upper lobe, lung
	44499676	Carcinoma, anaplastic, NOS, of lower lobe, lung
	44499678	Small cell carcinoma, NOS, of lower lobe, lung
	44499686	Adenoid cystic carcinoma of middle lobe, lung
	44500712	Combined small cell carcinoma of lower lobe, lung
	44500984	Squamous cell carcinoma, NOS, of upper lobe, lung
	44501707	Squamous cell carcinoma, keratinizing, NOS, of lung, NOS
	44501740	Carcinosarcoma, NOS, of lower lobe, lung
	44502769	Adenoid cystic carcinoma of lower lobe, lung
	44503111	Carcinosarcoma, NOS, of upper lobe, lung
	45769035	Primary carcinosarcoma of lung
	45938311	Metastatic Primary Lung Cancer
	45944435	Non-Small Cell Lung Cancer
NSCLC	45944435	Non-Small Cell Lung Cancer
	36684857	Metastatic non-small cell lung cancer
	4308479	Non-small cell carcinoma of lung, TNM stage 4
	4110705	Squamous cell carcinoma of lung
	4115276	Non-small cell lung cancer
	37109576	Squamous non-small cell lung cancer
	4110589	Large cell carcinoma of lung
	4112738	Adenocarcinoma of lung
	44501471	Non-small cell carcinoma of middle lobe, lung
	44500188	Non-small cell carcinoma of lower lobe, lung
	44499422	Non-small cell carcinoma of upper lobe, lung
SCLC	4110591	Small cell carcinoma of the lung
	4112739	Oat cell carcinoma of the lung
	36713366	Extensive stage primary small cell carcinoma of lung
	608926	Primary small cell carcinoma of left lung
	602160	Primary small cell carcinoma of left main bronchus
	608925	Primary small cell carcinoma of right lung
	605477	Primary small cell carcinoma of right main bronchus
	37395648	Primary small cell malignant neoplasm of lung, TNM stage 1
	37395649	Primary small cell malignant neoplasm of lung, TNM stage 2
	37395650	Primary small cell malignant neoplasm of lung, TNM stage 3
	37395651	Primary small cell malignant neoplasm of lung, TNM stage 4
	45768883	Primary small cell non-keratinizing squamous cell carcinoma of lung
	4110591	Small cell carcinoma of lung
	44499678	Small cell carcinoma, NOS, of lower lobe, lung

	44502159	Small cell carcinoma, NOS, of main bronchus
	44500000	Small cell carcinoma, NOS, of middle lobe, lung
	36521732	Small cell carcinoma, NOS, of overlapping lesion of lung
	44500483	Small cell carcinoma, NOS, of trachea
	44502427	Small cell carcinoma, NOS, of upper lobe, lung
	36713366	Extensive stage primary small cell carcinoma of lung
	608926	Primary small cell carcinoma of left lung
	602160	Primary small cell carcinoma of left main bronchus
	608925	Primary small cell carcinoma of right lung
	605477	Primary small cell carcinoma of right main bronchus
	37395648	Primary small cell malignant neoplasm of lung, TNM stage 1
	37395649	Primary small cell malignant neoplasm of lung, TNM stage 2
	37395650	Primary small cell malignant neoplasm of lung, TNM stage 3
	37395651	Primary small cell malignant neoplasm of lung, TNM stage 4
	45768883	Primary small cell non-keratinizing squamous cell carcinoma of lung
	44499678	Small cell carcinoma, NOS, of lower lobe, lung
	44502159	Small cell carcinoma, NOS, of main bronchus
	44500000	Small cell carcinoma, NOS, of middle lobe, lung
	36521732	Small cell carcinoma, NOS, of overlapping lesion of lung
	44500483	Small cell carcinoma, NOS, of trachea
	44502427	Small cell carcinoma, NOS, of upper lobe, lung
Colorectal; https://atlas-demo.ohdsi.org/#/cohortdefinition/1788623/conceptsets/	4180780	Malignant tumor of anal canal
	4198567	HNPCC - hereditary nonpolyposis colon cancer
	79740	Overlapping malignant neoplasm of colon
	197500	Primary malignant neoplasm of colon
	432257	Primary malignant neoplasm of transverse colon
	436635	Primary malignant neoplasm of sigmoid colon
	437798	Primary malignant neoplasm of splenic flexure of colon
	438979	Primary malignant neoplasm of hepatic flexure of colon
	441800	Primary malignant neoplasm of descending colon
	603310	Primary malignant gastrointestinal stromal neoplasm of colon
	761001	Primary malignant neuroendocrine neoplasm of ascending colon
	4089661	Malignant neoplasm, overlapping lesion of colon
	4092078	Malignant neoplasm of mesocolon
	4247360	Primary malignant neoplasm of the mesocolon
	4247719	Primary malignant neoplasm of ascending colon
	36683531	Malignant neoplasm of colon and/or rectum
	36715913	Primary malignant neuroendocrine neoplasm of colon
	37018659	Overlapping malignant neoplasm of colon and rectum
	435754	Malignant tumor of ascending colon

	443381	Malignant tumor of sigmoid colon
	443382	Malignant tumor of descending colon
	443384	Malignant tumor of transverse colon
	760957	Malignant carcinoid tumor of descending colon
	760958	Malignant carcinoid tumor of ascending colon
	4180790	Malignant tumor of colon
	37111620	Malignant carcinoid tumor of colon
	609194	Primary squamous cell carcinoma of skin of anus
	3655878	Neuroendocrine carcinoma of anus
	4309574	Adenocarcinoma of anus
	36716972	Primary squamous cell carcinoma of anus
	37016237	Primary adenocarcinoma of anus
	40487139	Carcinoma of skin of anus
	40489405	Carcinoma of anus
	4115028	Carcinoma of sigmoid colon
	4149847	Carcinoma of colon
	4193165	Carcinoma of descending colon
	4193871	Carcinoma of transverse colon
	4200514	Adenocarcinoma of sigmoid colon
	4207182	Carcinoma of ascending colon
	4307687	Carcinoma of colon, stage II
	4310858	Carcinoma of colon, stage III
	4312001	Carcinoma of colon, stage IV
	4312240	Carcinoma of colon, stage I
	35624316	Squamous cell carcinoma of colon
	36713361	Primary adenocarcinoma of ascending colon
	36715911	Primary adenocarcinoma of ascending colon and right flexure
	36715912	Primary adenocarcinoma of transverse colon
	36717181	Primary neuroendocrine carcinoma of colon
	36717495	Primary adenocarcinoma of descending colon and splenic flexure
	37208245	Primary adenocarcinoma of descending colon
	42872396	Primary adenocarcinoma of colon
	4110575	Adenocarcinoma of rectum
	35624314	Squamous cell carcinoma of rectum
	36717182	Primary neuroendocrine carcinoma of rectum
	40492939	Carcinoma of upper rectum
	4180791	Malignant tumor of hepatic flexure
	4180792	Malignant tumor of rectosigmoid junction
	4181344	Malignant tumor of splenic flexure
	443390	Malignant tumor of rectum
	40481902	Malignant neoplasm of anorectum
	40487050	Anorectal adenocarcinoma

	436348	Primary malignant neoplasm of anal canal
	4116241	Squamous cell carcinoma of anal margin
	35622690	Adenocarcinoma of anal canal
	4112143	Carcinoma of anal canal
	36715921	Primary cloacogenic carcinoma of anal canal
	36716511	Primary squamous cell carcinoma of anal canal
	37116449	Primary malignant neuroendocrine neoplasm of anal canal
	438699	Primary malignant neoplasm of rectosigmoid junction
	4151260	Carcinoma of the rectosigmoid junction
	37016239	Primary adenocarcinoma of rectosigmoid junction
	4095430	Malignant neoplasm of rectum, rectosigmoid junction and anus
	608050	Leiomyosarcoma of colon
	36715914	Primary malignant neuroendocrine neoplasm of rectum
	4112730	Malignant tumor of anorectal junction
	4322376	Adenocarcinoma of rectosigmoid junction
	603311	Primary malignant gastrointestinal stromal neoplasm of rectum
	37018934	Malignant carcinoid tumor of rectum
	74582	Primary malignant neoplasm of rectum
	438090	Overlapping malignant neoplasm of rectum, anus and anal canal
	608046	Leiomyosarcoma of rectum
	37116448	Primary malignant neuroendocrine neoplasm of anus
	80045	Primary malignant neoplasm of anus
	4180911	Malignant tumor of anus
	608069	Malignant mesenchymal neoplasm of anus
	432837	Primary malignant neoplasm of cecum
	433143	Primary malignant neoplasm of appendix
	443383	Malignant tumor of appendix
	443391	Malignant tumor of cecum
	443396	Malignant tumor of large intestine
	4116240	Carcinoma of cecum
	4184849	Adenocarcinoma of appendix
	4184850	Adenocarcinoma of cecum
	4196264	Metastasis from malignant tumor of colon
	4201618	Metastasis from malignant tumor of rectum
	4246125	Primary malignant neoplasm of large intestine
	4256776	Adenocarcinoma of large intestine
	36715890	Primary mucinous adenocarcinoma of appendix
	40492937	Carcinoma of appendix
Prostate; https://atlas-demo.ohdsi.org/#/cohortdefinition/1788649/conceptsets/	4163261	Malignant tumor of prostate
	37311236	Infiltrating duct carcinoma of prostate

	36716186	Hormone sensitive prostate cancer
	4116087	Carcinoma of prostate
	37395835	Familial prostate cancer
	4164017	Squamous cell carcinoma of prostate
	4082919	Endometrioid carcinoma of prostate
	37311683	Acinar cell cystadenocarcinoma of prostate
	4288534	Small cell carcinoma of prostate
	200962	Primary malignant neoplasm of prostate
	4141960	Hormone refractory prostate cancer
	4161028	Adenocarcinoma of prostate
	1553105	Adenosarcoma of prostate gland
	1553599	Adenocarcinoid tumor of prostate gland
	36519743	Adenocarcinoma in tubulovillous adenoma of prostate gland
	36529044	Papillary carcinoma, NOS, of prostate gland
	36530505	Adenocarcinoma with spindle cell metaplasia of prostate gland
	36531450	Squamous cell carcinoma, large cell, nonkeratinizing, NOS, of prostate gland
	36532395	Squamous cell carcinoma, microinvasive of prostate gland
	36532454	Squamous cell carcinoma, small cell, nonkeratinizing of prostate gland
	36534013	Squamous cell carcinoma, keratinizing, NOS, of prostate gland
	36534105	Squamous cell carcinoma with horn formation of prostate gland
	36535056	Adenocarcinoma with squamous metaplasia of prostate gland
	36543315	Squamous cell carcinoma, spindle cell of prostate gland
	36550033	Acinar cell cystadenocarcinoma of prostate gland
	36552560	Adenocarcinoma with apocrine metaplasia of prostate gland
	36553778	Verrucous carcinoma, NOS, of prostate gland
	36563396	Lymphoepithelial carcinoma of prostate gland
	36564577	Duct carcinoma, desmoplastic type of prostate gland
	36567202	Papillary squamous cell carcinoma of prostate gland
	36684947	Metastatic castration-resistant prostate cancer
	37016740	Prostate cancer metastatic to bone
	44499514	Infiltrating duct carcinoma, NOS, of prostate gland
	44499641	Papillary adenocarcinoma, NOS, of prostate gland
	44499712	Carcinoma, undifferentiated, NOS, of prostate gland
	44500716	Squamous cell carcinoma, adenoid of prostate gland
	44500734	Mixed cell adenocarcinoma of prostate gland
	44502000	Neoplasm, malignant of prostate gland
	44502766	Small cell carcinoma, NOS, of prostate gland
	44503133	Carcinoma, NOS, of prostate gland
	44503558	Adenosquamous carcinoma of prostate gland
Pancreas; https://atlas-demo.ohdsi.org/#/cohortde	602008	Primary adenocarcinoma of neck of pancreas

finition/1788647/conceptsets/		
	602011	Primary adenocarcinoma of tail of pancreas
	605820	Adenocarcinoma of pancreas with NRG1 fusion
	606747	Infiltrating duct carcinoma of pancreas
	3655584	Mucinous cystic neoplasm with invasive carcinoma of pancreas
	3655588	Mixed ductal-neuroendocrine carcinoma of pancreas
	4110585	Carcinoma of endocrine pancreas
	4157459	Carcinoma of pancreas
	4178960	Carcinoma of tail of pancreas
	4181331	Carcinoma of body of pancreas
	4209933	Carcinoma of head of pancreas
	4340498	Cystadenocarcinoma of pancreas
	36674768	Squamous cell carcinoma of exocrine pancreas
	36683250	Invasive intraductal papillary-mucinous carcinoma of pancreas
	36713362	Primary adenocarcinoma of body of pancreas
	36713363	Primary adenocarcinoma of head of pancreas
	37204187	Solid pseudopapillary carcinoma of pancreas
	37204808	Serous cystadenocarcinoma of pancreas
	37204852	Acinar cell carcinoma of pancreas
	37206235	Mucinous cystadenocarcinoma of pancreas
	42872399	Primary adenocarcinoma of pancreas
	45763891	Adenocarcinoma of pancreas
	765387	Malignant carcinoid tumour of pancreas
	4092072	Malignant tumour of body of pancreas
	4095436	Malignant tumour of tail of pancreas
	4112734	Malignant tumour of endocrine pancreas
	4111024	Malignant tumour of exocrine pancreas
	4180793	Malignant tumour of pancreas
	4178967	Malignant tumour of head of pancreas
	37311469	Pancreatic ductal adenocarcinoma
	192261	Overlapping malignant neoplasm of pancreas
	609180	Primary malignant gastrointestinal stromal neoplasm of pancreas
	37017016	Malignant insulinoma
	602009	Primary adenocarcinoma of pancreatic duct
	36715928	Primary adenocarcinoma of ampulla of Vater
	434293	Primary malignant neoplasm of body of pancreas
	432843	Primary malignant neoplasm of tail of pancreas
	4095437	Malignant tumour of Islets of Langerhans
	25486	Primary malignant neoplasm of islets of Langerhans
	36517463	Squamous cell carcinoma, small cell, nonkeratinizing of ampulla of Vater
	36518571	Squamous cell carcinoma, microinvasive of pancreatic duct

	36519758	Squamous cell carcinoma, keratinizing, NOS, of ampulla of Vater
	36520941	Solid pseudopapillary neoplasm of pancreas of body of pancreas
	36524367	Squamous cell carcinoma, large cell, nonkeratinizing, NOS, of ampulla of Vater
	36525341	Squamous cell carcinoma with horn formation of ampulla of Vater
	36531659	Squamous cell carcinoma, spindle cell of ampulla of Vater
	36532697	Infiltrating ductular carcinoma of pancreas, NOS
	36532856	Adenosquamous carcinoma of pancreatic duct
	36532986	Solid pseudopapillary neoplasm of pancreas of other specified parts of pancreas
	36533725	Squamous cell carcinoma, microinvasive of ampulla of Vater
	36535074	Squamous cell carcinoma, NOS, of pancreatic duct
	36536361	Squamous cell carcinoma, NOS, of ampulla of Vater
	36538588	Squamous cell carcinoma, small cell, nonkeratinizing of pancreatic duct
	36539200	Solid pseudopapillary neoplasm of pancreas of overlapping lesion of pancreas
	36541248	Verrucous carcinoma, NOS, of pancreatic duct
	36543806	Solid pseudopapillary neoplasm of pancreas of islets of Langerhans
	36544241	Squamous cell carcinoma, adenoid of pancreatic duct
	36545005	Squamous cell carcinoma with horn formation of pancreatic duct
	36547763	Squamous cell carcinoma, spindle cell of pancreatic duct
	36551753	Papillary squamous cell carcinoma of pancreatic duct
	36557175	Papillary squamous cell carcinoma of ampulla of Vater
	36559450	Squamous cell carcinoma, large cell, nonkeratinizing, NOS, of pancreatic duct
	36559572	Papillary carcinoma, NOS, of pancreatic duct
	36564146	Squamous cell carcinoma, keratinizing, NOS, of pancreatic duct
	36565792	Solid pseudopapillary neoplasm of pancreas of pancreatic duct
	36565876	Verrucous carcinoma, NOS, of ampulla of Vater
	36566781	Squamous cell carcinoma, adenoid of ampulla of Vater
	36567644	Solid pseudopapillary neoplasm of pancreas of head of pancreas
	44499628	Papillary carcinoma, NOS, of ampulla of Vater
	44499755	Adenosquamous carcinoma of ampulla of Vater
	44501527	Solid pseudopapillary neoplasm of pancreas of tail of pancreas
	36517463	Squamous cell carcinoma, small cell, nonkeratinizing of ampulla of Vater
	36518571	Squamous cell carcinoma, microinvasive of pancreatic duct
	36519758	Squamous cell carcinoma, keratinizing, NOS, of ampulla of Vater
	36520941	Solid pseudopapillary neoplasm of pancreas of body of pancreas
	36524367	Squamous cell carcinoma, large cell, nonkeratinizing, NOS, of ampulla of Vater
	36525341	Squamous cell carcinoma with horn formation of ampulla of Vater
	36531659	Squamous cell carcinoma, spindle cell of ampulla of Vater
	4094866	Malignant tumor of pancreatic duct

	433423	Primary malignant neoplasm of pancreatic duct
	199754	Primary malignant neoplasm of pancreas
	601133	Primary malignant neoplasm of neck of pancreas
	36567644	Solid pseudopapillary neoplasm of pancreas of head of pancreas
	44499628	Papillary carcinoma, NOS, of ampulla of Vater
	44499755	Adenosquamous carcinoma of ampulla of Vater
	44501527	Solid pseudopapillary neoplasm of pancreas of tail of pancreas
	40391739	Pancreatoblastoma
	37395837	Familial malignant neoplasm of pancreas
	440649	Primary malignant neoplasm of head of pancreas
	4092074	Malignant neoplasm of ectopic pancreatic tissue
	42536743	Primary malignant neuroendocrine neoplasm of pancreas
Ovary; https://atlas-demo.ohdsi.org/#/cohortdefinition/1788646/conceptsets/	4307838	Ovarian cancer, disseminated
	36674976	Hereditary site-specific ovarian cancer syndrome
	37397555	Hereditary breast and ovarian cancer syndrome
	4112860	Brenner tumor of ovary
	4300688	Yolk sac tumor
	4110865	Theca cell tumor of ovary
	4112079	Sertoli-Leydig cell tumor of ovary
	4112864	Malignant germ cell tumor of ovary
	4116073	Malignant epithelial tumor of ovary
	4116074	Malignant sex cord tumor of ovary
	4181351	Malignant tumor of ovary
	4240443	T1c (IC): Tumor limited to one or both ovaries
	4265308	pT1c (IC): Tumor limited to one or both ovaries
	4110863	Undifferentiated carcinoma of ovary
	4310444	Carcinoma of ovary, stage 4
	4311462	Carcinoma of ovary, stage 2
	4311576	Carcinoma of ovary, stage 1
	4313202	Carcinoma of ovary, stage 3
	4112862	Granulosa cell tumor of ovary
	4116077	Dysgerminoma of ovary
	36686093	Malignant germ cell neoplasm of right ovary
	36686094	Malignant germ cell neoplasm of left ovary
	37396882	Theca steroid producing cell malignant neoplasm of ovary
	4116076	Embryonal carcinoma of ovary
	4112865	Choriocarcinoma of ovary
	4110870	Endodermal sinus tumor of ovary
	37396690	Primary non-gestational choriocarcinoma of ovary
	37311080	Malignant immature teratoma of ovary

	37116598	Primary mucinous adenocarcinoma of ovary
	4112857	Endometrioid carcinoma ovary
	602307	Left ovarian primary mucinous cystadenocarcinoma
	602311	Left ovarian primary endometrioid carcinoma
	602310	Right ovarian primary endometrioid carcinoma
	4112856	Mucinous cystadenocarcinoma of ovary
	4198275	Cystadenocarcinoma of ovary
	36674767	Small cell carcinoma of ovary
	35621826	Clear cell adenocarcinoma of ovary
	602306	Right ovarian primary mucinous cystadenocarcinoma
	36716618	Primary high grade serous adenocarcinoma of ovary
	200051	Primary malignant neoplasm of ovary
	36687125	Carcinosarcoma of bilateral ovaries
	4283749	Malignant tumor involving right ovary by direct extension from left ovary
	4289682	Malignant tumor involving left ovary by direct extension from right ovary
	4112855	Serous papillary cystadenocarcinoma ovary
	4289681	Primary malignant neoplasm of left ovary
	36687124	Carcinosarcoma of right ovary
	4289392	Primary malignant neoplasm of right ovary
	45765433	Carcinosarcoma of ovary
	36717228	Primary low grade serous adenocarcinoma of ovary
	4307986	Sarcoma of ovary
	602308	Primary serous papillary cystadenocarcinoma of right ovary
	36687123	Carcinosarcoma of left ovary
	602309	Primary serous papillary cystadenocarcinoma of left ovary
	608868	Right ovarian primary sarcoma
	608867	Left ovarian primary sarcoma
	3177517	Metastatic adenocarcinoma of ovary
	35622945	Fibrothecoma of ovary
	36517655	Teratocarcinoma of ovary
	36529012	Polyembryoma of ovary
	36546343	Mucinous carcinoma, gastric type of ovary
	36549316	Malignant teratoma, undifferentiated of ovary
	36554907	Malignant teratoma, intermediate of ovary
	44499578	Germ cell tumor, nonseminomatous of ovary
	44500162	Teratoma, malignant, NOS, of ovary
	44502582	Seminoma, NOS, of ovary
	44502731	Teratoma with malignant transformation of ovary
	44502732	Struma ovarii, malignant of ovary
	44503047	Mixed germ cell tumor of ovary
	44829813	Malignant neoplasm of ovary and other uterine adnexa

	45459701	Malignant neoplasm of ovary and other uterine adnexa
Leukaemia; https://atlas-demo.ohdsi.org/#/cohortdefinition/1788635/conceptsets/	132853	Lymphoid leukaemia
	134305	Acute lymphoid leukaemia
	134603	Chronic myeloid leukaemia
	135499	Subacute myeloid leukaemia
	135768	Acute monocytic leukaemia
	136056	Chronic monocytic leukaemia
	136656	Subacute lymphoid leukaemia
	138099	Erythroleukaemia, FAB M6
	138379	Chronic lymphoid leukaemia, disease
	138708	Acute leukaemia
	140057	Chronic leukaemia
	140352	Acute myeloid leukaemia, disease
	140666	Myeloid leukaemia
	313159	Megakaryocytic leukaemia
	313430	Subacute monocytic leukaemia
	315497	Subacute leukaemia
	317510	Leukaemia
	321526	Monocytic leukaemia
	600661	Mixed phenotype acute leukaemia with T-cell and myeloid lineage
	600663	Mixed phenotype acute leukaemia with myeloid and B-cell lymphoid phenotypes
	606958	Acute myeloid leukaemia with t(8;21)(q22;q22) RUNX1-RUNX1T1
	607405	Mixed phenotype acute leukaemia with t(9;22) (q34;q11.2); BCR-ABL1
	608277	Acute myeloid leukaemia with 11q23 abnormality
	3654662	Acute myeloid leukaemia with inv(16)(p13.1q22) or t(16;16)(p13.1;q22) CBFB-MYH11
	3654647	B lymphoblastic leukaemia lymphoma with t(5;14)(q31;q32); IL3-IGH
	3654648	B lymphoblastic leukaemia lymphoma with t(v;11q23); MLL rearranged
	3654649	B lymphoblastic leukaemia lymphoma with t(12;21) (p13;q22); TEL/AML1 (ETV6-RUNX1)
	3654650	B lymphoblastic leukaemia lymphoma with t(1;19)(Q23;P13.3); E2A-PBX1 (TCF3/PBX1)
	3654651	B lymphoblastic leukaemia lymphoma with hypodiploidy
	3654653	B lymphoblastic leukaemia lymphoma with hyperdiploidy
	4001331	Prolymphocytic leukaemia (clinical)
	4002496	Mast cell leukaemia (clinical)
	4002497	Acute promyelocytic leukaemia, FAB M3
	4003187	Acute myelomonocytic leukaemia, FAB M4
	4003188	Adult T-cell leukaemia/lymphoma
	4038845	Hairy cell leukaemia (clinical)

	4079281	Null cell acute lymphoblastic leukaemia
	4079280	Common acute lymphoblastic leukaemia
	4079282	Atypical chronic myeloid leukaemia
	4079683	T-cell prolymphocytic leukaemia
	4079686	Acute megakaryoblastic leukaemia
	4079690	Prethymic and thymic T-cell lymphoma/leukaemia
	4081867	Acute biphenotypic leukaemia
	4082311	B-cell chronic lymphocytic leukaemia
	4082459	Hairy cell leukaemia variant
	4082460	Large granular lymphocytic leukaemia
	4082461	Precursor B-cell acute lymphoblastic leukaemia
	4082462	T-cell acute lymphoblastic leukaemia
	4082338	Chronic lymphocytic prolymphocytic leukaemia syndrome
	4082481	Juvenile chronic myeloid leukaemia
	4082485	Acute monoblastic leukaemia
	4091925	Chronic eosinophilic leukaemia
	4094549	Aleukemic lymphoid leukaemia
	4094550	Adult T-cell leukaemia
	4094553	Aleukemic monocytic leukaemia
	4095897	Compound leukaemias
	4097581	Chronic neutrophilic leukaemia
	4097585	Aleukemic myeloid leukaemia
	4097706	Myelomonocytic leukaemia
	4097707	Subacute myelomonocytic leukaemia
	4112803	Acute promyelocytic leukaemia - hypogranular variant
	4116880	Acute myelomonocytic leukaemia - eosinophilic variant
	4121332	Aleukemic leukaemia
	4133599	Chronic myelomonocytic leukaemia
	4138008	Philadelphia chromosome-positive acute lymphoblastic leukaemia
	4139554	Atypical hairy cell leukaemia
	4144191	Basophilic leukaemia
	4146022	Neutrophilic leukaemia
	4153344	Acute lymphoblastic leukaemia, transitional pre-B-cell
	4173824	B-cell chronic lymphocytic leukaemia variant
	4173955	T-cell chronic lymphocytic leukaemia
	4173963	B-cell acute lymphoblastic leukaemia
	4173970	Acute eosinophilic leukaemia
	4173974	B-cell prolymphocytic leukaemia
	4175688	Hypergranular promyelocytic leukaemia
	4185301	Chronic myeloid leukaemia in myeloid blast crisis
	4187635	Accelerated phase chronic myeloid leukaemia
	4188973	Chronic myeloid leukaemia in lymphoid blast crisis

	4188975	Chronic phase chronic myeloid leukaemia
	4189938	Acute monocytic/monoblastic leukaemia
	4211481	Blastic phase chronic myeloid leukaemia
	4221907	Precursor T cell lymphoblastic leukaemia/lymphoblastic lymphoma
	4230253	Acute myeloid leukaemia without maturation, FAB M1
	4233531	Acute myeloid leukaemia, minimal differentiation, FAB M0
	4234749	Acute myeloid leukaemia with maturation, FAB M2
	4245460	Hairy cell leukaemia of spleen
	4297353	Leukemic infiltration of skin (chronic T-cell lymphocytic leukaemia)
	4297355	Aggressive NK-cell leukaemia involving skin
	4299143	Leukemic infiltration of skin (T-cell lymphoblastic leukaemia)
	4299273	Mast cell leukaemia affecting skin
	4299151	Leukemic infiltration of skin in hairy-cell leukaemia
	4299153	Leukemic infiltration of skin in myeloid leukaemia
	4299154	Leukemic infiltration of skin in chronic myeloid leukaemia
	4299155	Leukemic infiltration of skin in monocytic leukaemia
	4300784	Leukemic infiltration of skin in acute myeloid leukaemia
	4301665	Leukemic infiltration of skin (T-cell prolymphocytic leukaemia)
	4326339	Smoldering chronic lymphocytic leukaemia
	35607963	Megakaryoblastic acute myeloid leukaemia with t(1;22)(p13;q13)
	35622003	Acute myeloid leukaemia with NPM1 somatic mutation
	35622696	Acute myeloid leukaemia with CEBPA somatic mutations
	35622760	Inherited acute myeloid leukaemia
	35623630	Acute myeloid leukaemia and myelodysplastic syndrome related to alkylating agent
	35623631	Acute myeloid leukaemia and myelodysplastic syndrome related to topoisomerase type 2 inhibitor
	35623633	Acute myeloid leukaemia and myelodysplastic syndrome related to radiation
	36674687	Aleukemic mast cell leukaemia
	36676614	Differentiation syndrome due to and following chemotherapy co-occurrent with acute promyelocytic leukaemia
	36683269	Acute myeloid leukaemia with inv(3)(q21q26.2) or t(3;3)(q21;q26.2); RPN1-EVI1
	36715966	Adult T-cell leukaemia/lymphoma of skin
	36715587	Acute myeloid leukaemia due to recurrent genetic abnormality
	36715589	Acute leukaemia of ambiguous lineage
	36717231	Meningeal leukaemia
	36717461	Therapy related acute myeloid leukaemia and myelodysplastic syndrome
	36717161	Aggressive natural killer-cell leukaemia
	37017893	Philadelphia chromosome-negative precursor B-cell acute lymphoblastic leukaemia
	37018869	Disorder of central nervous system co-occurrent and due to acute lymphoid leukaemia

	37109936	B lymphoblastic leukaemia lymphoma with t(9:22) (q34;q11.2); BCR-ABL 1
	37110870	Acute myeloid leukaemia with t(8;16)(p11;p13) translocation
	37110902	Chronic lymphocytic leukaemia genetic mutation variant
	37116722	Acute myeloid leukaemia with t(6;9)(p23;q34) translocation
	37119145	Myeloid leukaemia co-occurrent with Down syndrome
	37204530	Non-chronic lymphocytic leukaemia monoclonal B-cell lymphocytosis
	37204479	Noonan syndrome-like disorder with juvenile myelomonocytic leukaemia
	37206728	Monoclonal B-cell lymphocytosis chronic lymphocytic leukaemia-type
	40481524	Acute myeloid leukaemia with t(9:11)(p22;q23); MLLT3-MLL
	40482847	Juvenile myelomonocytic leukaemia
	40483761	Acute myeloid leukaemia with myelodysplasia-related changes
	40486741	Philadelphia chromosome negative chronic myelogenous leukaemia
	40493442	Philadelphia chromosome positive chronic myelogenous leukaemia
	42538579	Therapy related acute myeloid leukaemia due to and following administration of antineoplastic agent
	42539431	Acute myeloid leukaemia with FMS-like tyrosine kinase-3 mutation
	44783718	T-cell large granular lymphocytic leukaemia
	45766268	Cytogenetically normal acute myeloid leukaemia
	45767656	Gingivitis due to leukaemia
	45765495	Core binding factor acute myeloid leukaemia
	46271363	Periodontitis co-occurrent with leukaemia
	4301780	Leukemic infiltration of skin
	44784140	Emberger syndrome
	132570	Leukemic reticuloendotheliosis of lymph nodes of head, face and neck
	193429	Leukemic reticuloendotheliosis of intra-abdominal lymph nodes
	44814026	Clinical stage C chronic lymphocytic leukaemia
	132852	Leukemic reticuloendotheliosis of extranodal AND/OR solid organ site
	44811228	Clinical stage B chronic lymphocytic leukaemia
	439269	Leukemic reticuloendotheliosis of lymph nodes of axilla and upper limb
	318989	Leukemic reticuloendotheliosis of lymph nodes of multiple sites
	442095	Leukemic reticuloendotheliosis of intrathoracic lymph nodes
	439268	Leukemic reticuloendotheliosis of lymph nodes of inguinal region and lower limb
	196650	Leukemic reticuloendotheliosis of intrapelvic lymph nodes
	44811227	Clinical stage A chronic lymphocytic leukaemia
	44807009	Acute myeloid leukaemia with 11q23 abnormality
	4097582	Chloroma
	4227963	Precursor T-cell lymphoblastic lymphoma
	4298848	T-cell leukemic infiltration of skin
	3046363	Acute leukaemia markers [Interpretation] in Specimen Narrative
	4028713	Acute myeloid leukaemia, t(8;21) (q22;q22)

	4028862	Chronic leukaemia (category)
	4028863	Lymphoid leukaemia (category)
	4029176	Chronic myelogenous leukaemia, BCR/ABL positive
	4029177	Acute myeloid leukaemia with myelodysplasia-related changes
	4029206	Myeloid leukaemia (category)
	4029663	Acute myeloid leukaemia, 11q23 abnormalities
	4029800	Prolymphocytic leukaemia
	4030263	Therapy-related acute myeloid leukaemia and myelodysplastic syndrome
	4030264	Chronic myelomonocytic leukaemia
	4030289	Leukaemia (category)
	4031360	Acute myeloid leukaemia, M6 type
	4073533	Acute myeloid leukaemia, no ICD-O subtype
	4080746	Acute leukaemia
	4095898	Eosinophilic leukaemia
	4103718	Acute promyelocytic leukaemia
	4138686	Lymphoid leukaemia
	4149110	Acute myelomonocytic leukaemia
	4180093	Chronic lymphocytic leukaemia
	4180418	Acute megakaryoblastic leukaemia
	4182216	Hairy cell leukaemia
	4184848	Acute myeloid leukaemia
	4213196	Acute panmyelosis with myelofibrosis
	4264447	Acute myeloid leukaemia with multilineage dysplasia following a myelodysplastic syndrome or myelodysplastic syndrome/myeloproliferative disorder
	4265011	Acute myeloid leukaemia with recurrent genetic abnormality
	4272001	Chronic myeloid leukaemia
	4288090	Acute myeloid leukaemia with multilineage dysplasia without antecedent myelodysplastic syndrome
	4289318	Acute basophilic leukaemia
	4295361	Myeloid leukaemia
	4304051	Acute myeloid leukaemia with maturation
	4304199	Acute myeloid leukaemia, minimal differentiation
	4304356	Acute myeloid leukaemia without maturation
	4314535	Leukaemia
	4319135	Burkitt cell leukaemia
	37110871	Acute myeloid leukaemia with t(8;16)(p11;p13) translocation
	37204375	Acute myeloid leukaemia with BCR-ABL1
	37204557	Acute myeloid leukaemia with mutated RUNX1
	37312067	Acute myeloid leukaemia with biallelic mutation of CEBPA (CCAAT enhancer binding protein alpha) gene
	37312109	Monoclonal B-cell lymphocytosis non-chronic lymphocytic leukaemia type

	37312112	Monoclonal B-cell lymphocytosis chronic lymphocytic leukaemia-type
	42535969	Acute myeloid leukaemia with FMS-like tyrosine kinase-3 mutation
	42616301	Chronic eosinophilic leukaemia [hypereosinophilic syndrome]
	42872921	Mixed phenotype acute leukaemia B/myeloid
	42872922	Mixed phenotype acute leukaemia T/myeloid
	42872933	Acute myeloid leukaemia with t(6;9)(p23;q34); DEK-NUP214
	42872934	Acute myeloid leukaemia with inv(3)(q21q26.2) or t(3;3)(q21;q26.2); RPN1-EVI1
	42872942	Acute myeloid leukaemia (megakaryoblastic) with t(1;22)(p13;q13); RBM15-MKL1
	44502507	Acute myeloid leukaemia, t(8;21)(q22;q22) of bone marrow
	44504695	Precursor B-cell lymphoblastic leukaemia of bone marrow
	44504715	Chronic myelomonocytic leukaemia, NOS, of bone marrow
	45423305	[M]Leukaemia unspecified, NOS
	45429895	[M]Chronic lymphoid leukaemia
	45429896	[M]Miscellaneous leukaemias
	45433185	[M]Blast cell leukaemia
	45433186	[M]Prolymphocytic leukaemia
	45433187	[M]Acute megakaryoblastic leukaemia
	45436510	[M]Stem cell leukaemia
	45436511	[M]Lymphoid leukaemias
	45436513	[M]Thrombocytic leukaemia
	45443080	[M]Lymphoid leukaemia NOS
	45453093	[M]Leukaemias
	45453095	[M]Hairy cell leukaemia
	45456446	[M]Chronic leukaemia NOS
	45456448	[M]Acute myelomonocytic leukaemia
	45459803	[M]Granulocytic leukaemia NOS
	45459804	[M]Eosinophilic leukaemia NOS
	45463246	[M]Acute leukaemia NOS
	45463247	[M]Chronic myeloid leukaemia
	45463248	[M]Chloroma
	45463249	[M]Acute myelofibrosis
	45470035	[M]Acute erythraemia
	45470036	[M]Acute promyelocytic leukaemia
	45470037	[M]Other myeloid leukaemia NOS
	45473321	[M]Leukaemia NOS
	45473323	[M]Basophilic leukaemia
	45476713	[M]Acute myeloid leukaemia
	45483220	Megakaryocytic leukaemia
	45483308	[M]Myeloid leukaemia NOS
	45483309	[M]Chronic myelomonocytic leukaemia
	45486667	[M]Subacute leukaemia NOS

	45486669	[M]Myeloid leukaemias
	45486670	[M]Schilling-type monocytic leukaemia
	45486671	[M]Leukaemia NOS
	45489942	[M]Blastic leukaemia
	45493139	Subacute myelomonocytic leukaemia
	45493209	[M]Leukaemias unspecified
	45493214	[M]Naegeli-type monocytic leukaemia
	45499846	[M]Lymphatic leukaemia
	45503160	[M]Neutrophilic leukaemia
	45516597	[M]Acute lymphoid leukaemia
	45519829	[M]Miscellaneous leukaemia NOS
	45523071	Adult T-cell leukaemia
	45523131	[M]Burkitt's cell leukaemia
	45523133	[M]Eosinophilic leukaemias
	45523134	[M]Chronic monocytic leukaemia
	45766616	Acute myeloid leukaemia with mutated NPM1
	45771384	Acute myeloid leukaemia with mutation of CEBPA (CCAAT enhancer binding protein alpha) gene
Acute Myeloid Leukaemia	140352	Acute myeloid leukaemia, disease
	44807009	Acute myeloid leukaemia with 11q23 abnormality
	135499	Subacute myeloid leukaemia
	4233531	Acute myeloid leukaemia, minimal differentiation, FAB M0
	4230253	Acute myeloid leukaemia without maturation, FAB M1
	4234749	Acute myeloid leukaemia with maturation, FAB M2
	4300784	Leukemic infiltration of skin in acute myeloid leukaemia
	40481524	Acute myeloid leukaemia with t(9:11)(p22;q23); MLLT3-MLL
	40483761	Acute myeloid leukaemia with myelodysplasia-related changes
	45765495	Core binding factor acute myeloid leukaemia
	45766268	Cytogenetically normal acute myeloid leukaemia
	36715587	Acute myeloid leukaemia due to recurrent genetic abnormality
	36717461	Therapy related acute myeloid leukaemia and myelodysplastic syndrome
	37110870	Acute myeloid leukaemia with t(8;16)(p11;p13) translocation
	37116722	Acute myeloid leukaemia with t(6;9)(p23;q34) translocation
	42539431	Acute myeloid leukaemia with FMS-like tyrosine kinase-3 mutation
	35622003	Acute myeloid leukaemia with NPM1 somatic mutation
	35607963	Megakaryoblastic acute myeloid leukaemia with t(1;22)(p13;q13)
	35622696	Acute myeloid leukaemia with CEBPA somatic mutations
	35622760	Inherited acute myeloid leukaemia
	36683269	Acute myeloid leukaemia with inv(3)(q21q26.2) or t(3;3)(q21;q26.2); RPN1-EVI1
	3654662	Acute myeloid leukaemia with inv(16)(p13.1q22) or t(16;16)(p13.1;q22) CBFB-MYH11
	4002497	Acute promyelocytic leukaemia, FAB M3

	4112803	Acute promyelocytic leukaemia - hypogranular variant
	4175688	Hypergranular promyelocytic leukaemia
	4116880	Acute myelomonocytic leukaemia - eosinophilic variant
	4079686	Acute megakaryoblastic leukaemia
	138099	Erythroleukaemia, FAB M6
	4144191	Basophilic leukaemia
	4003187	Acute myelomonocytic leukaemia, FAB M4
	135768	Acute monocytic leukaemia
	4003184	Acute panmyelosis with myelofibrosis
	4082485	Acute monoblastic leukaemia
	4189938	Acute monocytic/monoblastic leukaemia
	4173970	Acute eosinophilic leukaemia
	4304355	Acute myeloid leukaemia with abnormal marrow eosinophils
	4304199	Acute myeloid leukaemia, minimal differentiation
	4304356	Acute myeloid leukaemia without maturation
	4304051	Acute myeloid leukaemia with maturation
	4029177	Acute myeloid leukaemia with myelodysplasia-related changes
	4028713	Acute myeloid leukaemia, t(8;21) (q22;q22)
	4029663	Acute myeloid leukaemia, 11q23 abnormalities
	4030263	Therapy-related acute myeloid leukaemia and myelodysplastic syndrome
	4031360	Acute myeloid leukaemia, M6 type
	4073533	Acute myeloid leukaemia, no ICD-O subtype
	4265011	Acute myeloid leukaemia with recurrent genetic abnormality
	4264447	Acute myeloid leukaemia with multilineage dysplasia following a myelodysplastic syndrome or myelodysplastic syndrome/myeloproliferative disorder
	4288090	Acute myeloid leukaemia with multilineage dysplasia without antecedent myelodysplastic syndrome
	4184848	Acute myeloid leukaemia
	42872921	Mixed phenotype acute leukaemia B/myeloid
	42872922	Mixed phenotype acute leukaemia T/myeloid
	42872933	Acute myeloid leukaemia with t(6;9)(p23;q34); DEK-NUP214
	42872934	Acute myeloid leukaemia with inv(3)(q21q26.2) or t(3;3)(q21;q26.2); RPN1-EVI1
	42872942	Acute myeloid leukaemia (megakaryoblastic) with t(1;22)(p13;q13); RBM15-MKL1
	45771384	Acute myeloid leukaemia with mutation of CEBPA (CCAAT enhancer binding protein alpha) gene
	45766616	Acute myeloid leukaemia with mutated NPM1
	37110871	Acute myeloid leukaemia with t(8;16)(p11;p13) translocation
	42535969	Acute myeloid leukaemia with FMS-like tyrosine kinase-3 mutation
	37204375	Acute myeloid leukaemia with BCR-ABL1
	37204557	Acute myeloid leukaemia with mutated RUNX1

	37312067	Acute myeloid leukaemia with biallelic mutation of CEBPA (CCAAT enhancer binding protein alpha) gene
Chronic Myeloid Leukaemia	134603	Chronic myelocytic leukaemia
	4187635	Accelerated phase chronic myeloid leukaemia
	4079282	Atypical chronic myeloid leukaemia
	4211481	Blastic phase chronic myeloid leukaemia
	36402753	Chronic myelogenous leukaemia, BCR/ABL positive of blood
	44501329	Chronic myelogenous leukaemia, BCR/ABL positive of bone marrow
	36563942	Chronic myelogenous leukaemia, BCR/ABL positive of hematopoietic system, NOS
	36547897	Chronic myelogenous leukaemia, BCR/ABL positive of reticuloendothelial system, NOS
	134603	Chronic myeloid leukaemia
	4188973	Chronic myeloid leukaemia in lymphoid blast crisis
	4185301	Chronic myeloid leukaemia in myeloid blast crisis
	4097581	Chronic neutrophilic leukaemia
	4188975	Chronic phase chronic myeloid leukaemia
	4082481	Juvenile chronic myeloid leukaemia
	40482847	Juvenile myelomonocytic leukaemia
	4299154	Leukemic infiltration of skin in chronic myeloid leukaemia
	40486741	Philadelphia chromosome negative chronic myelogenous leukaemia
	40493442	Philadelphia chromosome positive chronic myelogenous leukaemia
Acute lymphoblastic leukaemia	134305	Acute lymphoid leukaemia
	136656	Subacute lymphoid leukaemia
	37018869	Disorder of central nervous system co-occurrent and due to acute lymphoid leukaemia
	4173963	B-cell acute lymphoblastic leukaemia
	4082461	Precursor B-cell acute lymphoblastic leukaemia
	4079280	Common acute lymphoblastic leukaemia
	4079281	Null cell acute lymphoblastic leukaemia
	4082462	T-cell acute lymphoblastic leukaemia
	4153344	Acute lymphoblastic leukaemia, transitional pre-B-cell
	4299143	Leukemic infiltration of skin (T-cell lymphoblastic leukaemia)
	4221907	Precursor T cell lymphoblastic leukaemia/lymphoblastic lymphoma
	4138008	Philadelphia chromosome-positive acute lymphoblastic leukaemia
	37017893	Philadelphia chromosome-negative precursor B-cell acute lymphoblastic leukaemia
	37109936	B lymphoblastic leukaemia lymphoma with t(9:22) (q34;q11.2); BCR-ABL 1
	3654647	B lymphoblastic leukaemia lymphoma with t(5;14)(q31;q32); IL3-IGH
	3654648	B lymphoblastic leukaemia lymphoma with t(v;11q23); MLL rearranged
	3654649	B lymphoblastic leukaemia lymphoma with t(12;21) (p13;q22); TEL/AML1 (ETV6-RUNX1)

	3654650	B lymphoblastic leukaemia lymphoma with t(1;19)(Q23;P13.3); E2A-PBX1 (TCF3/PBX1)
	3654651	B lymphoblastic leukaemia lymphoma with hypodiploidy
	3654653	B lymphoblastic leukaemia lymphoma with hyperdiploidy
	4003188	Adult T-cell leukaemia/lymphoma
	4081867	Acute biphenotypic leukaemia
	4227963	Precursor T-cell lymphoblastic lymphoma
	4030260	Precursor cell lymphoblastic leukaemia
	4029662	Precursor B-cell lymphoblastic leukaemia
	4030261	Precursor T-cell lymphoblastic leukaemia
	4264448	Precursor B-lymphoblastic leukaemia/lymphoblastic lymphoma
	4288091	Precursor T cell lymphoblastic leukaemia/lymphoblastic lymphoma
	4189936	Acute lymphoblastic leukaemia - category
	4143821	Philadelphia chromosome-positive acute lymphoblastic leukaemia
	42872925	B lymphoblastic leukaemia / lymphoma - category
	42872954	B lymphoblastic leukaemia lymphoma, no ICD-O subtype
	42872955	B lymphoblastic leukaemia lymphoma with t(9;22)(q34;q11.2); BCR-ABL1
	42872956	B lymphoblastic leukaemia lymphoma with t(v;11q23); MLL rearranged
	42872957	B lymphoblastic leukaemia lymphoma with t(12;21)(p13;q22); TEL-AML1 (ETV6-RUNX1)
	42872958	B lymphoblastic leukaemia lymphoma with hyperdiploidy
	42872959	B lymphoblastic leukaemia lymphoma with hypodiploidy (Hypodiploid ALL)
	42872960	B lymphoblastic leukaemia lymphoma with t(5;14)(q31;q32); IL3-IGH
	42872961	B lymphoblastic leukaemia lymphoma with t(1;19)(q23;p13.3); E2A-PBX1 (TCF3-PBX1)
	45766617	T lymphoblastic leukaemia/lymphoma
	37204662	NK-lymphoblastic leukaemia/lymphoma
	37204838	B-lymphoblastic leukaemia lymphoma BCR-ABL1-like
	37206196	B lymphoblastic leukaemia lymphoma with iAMP21
Chronic lymphoblastic leukaemia	138379	Chronic lymphoid leukaemia
	44811228	Clinical stage B chronic lymphocytic leukaemia
	44814026	Clinical stage C chronic lymphocytic leukaemia
	4082311	B-cell chronic lymphocytic leukaemia
	4173824	B-cell chronic lymphocytic leukaemia variant
	4173955	T-cell chronic lymphocytic leukaemia
	4082338	Chronic lymphocytic prolymphocytic leukaemia syndrome
	4297353	Leukemic infiltration of skin (chronic T-cell lymphocytic leukaemia)
	4326339	Smoldering chronic lymphocytic leukaemia
	37110902	Chronic lymphocytic leukaemia genetic mutation variant
	37206728	Monoclonal B-cell lymphocytosis chronic lymphocytic leukaemia-type
	138379	Chronic lymphoid leukaemia, disease

	44783718	T-cell large granular lymphocytic leukaemia
	132570	Leukemic reticuloendotheliosis of lymph nodes of head, face and neck
	4082460	Large granular lymphocytic leukaemia
	193429	Leukemic reticuloendotheliosis of intra-abdominal lymph nodes
	4173974	B-cell prolymphocytic leukaemia
	132852	Leukemic reticuloendotheliosis of extranodal AND/OR solid organ site
	4082459	Hairy cell leukaemia variant
	4299151	Leukemic infiltration of skin in hairy-cell leukaemia
	4001331	Prolymphocytic leukaemia (clinical)
	4245460	Hairy cell leukaemia of spleen
	4139554	Atypical hairy cell leukaemia
	439269	Leukemic reticuloendotheliosis of lymph nodes of axilla and upper limb
	4038845	Hairy cell leukaemia (clinical)
	318989	Leukemic reticuloendotheliosis of lymph nodes of multiple sites
	4079683	T-cell prolymphocytic leukaemia
	439268	Leukemic reticuloendotheliosis of lymph nodes of inguinal region and lower limb
	196650	Leukemic reticuloendotheliosis of intrapelvic lymph nodes
	442095	Leukemic reticuloendotheliosis of intrathoracic lymph nodes
	4180093	Chronic lymphocytic leukaemia
	37312112	Monoclonal B-cell lymphocytosis chronic lymphocytic leukaemia-type
	37312109	Monoclonal B-cell lymphocytosis non-chronic lymphocytic leukaemia type
	4186899	Chronic lymphoid leukaemia - category
Multiple Myeloma	4224628	Amyloid light chain amyloidosis due to multiple myeloma
	4258135	Asymptomatic multiple myeloma
	4043447	Bone marrow: myeloma cells
	4094548	Extramedullary plasmacytoma
	37209514	Hypogammaglobulinemia due to multiple myeloma
	4111355	IgA myeloma
	4112310	IgD myeloma
	4111356	IgG myeloma
	4259972	Indolent multiple myeloma
	4188299	Kappa light chain myeloma
	4197600	Lambda light chain myeloma
	4082464	Light chain myeloma
	37016161	Light chain nephropathy due to multiple myeloma
	437233	Multiple myeloma
	4210177	Multiple myeloma
	4214660	Multiple solitary plasmacytomas
	4019477	Myeloma-associated amyloidosis
	4137433	Myeloma kidney

	4043713	Neuropathy due to multiple myeloma
	4079684	Non-secretory myeloma
	42538151	Osteoporosis co-occurrent and due to multiple myeloma
	4137510	Osteosclerotic myeloma
	133154	Plasma cell leukaemia
	4028859	Plasma cell leukaemia
	4190641	Plasma cell myeloma - category
	4190642	Plasma cell myeloma/plasmacytoma
	4163558	Plasma cell myeloma/plasmacytoma
	4216139	Plasmacytoma
	4024874	Plasmacytoma
	4300702	Primary cutaneous plasmacytoma
	4184985	Smoldering myeloma
	4145040	Solitary osseous myeloma
Breast; https://atlas-demo.ohdsi.org/#/cohortdefinition/1788621/conceptsets/	759932	Infiltrating duct carcinoma of left female breast
	759933	Infiltrating duct carcinoma of right female breast
	761170	Infiltrating duct carcinoma of bilateral female breasts
	4237178	Infiltrating duct carcinoma of breast
	37017351	Invasive carcinoma of breast
	3179883	Invasive carcinoma of breast without extensive intraductal component
	3184724	Invasive carcinoma of breast with extensive intraductal component
	4116071	Carcinoma of breast (disorder)
	36712719	Infiltrating ductal carcinoma of upper inner quadrant of left female breast
	36712720	Infiltrating ductal carcinoma of upper outer quadrant of left female breast
	36712721	Infiltrating ductal carcinoma of central portion of right female breast
	36712722	Infiltrating ductal carcinoma of upper inner quadrant of right female breast
	36712723	Infiltrating ductal carcinoma of upper outer quadrant of right female breast
	36712724	Infiltrating lobular carcinoma of left female breast
	36712725	Infiltrating lobular carcinoma of right female breast
	36717260	Infiltrating ductal carcinoma of central portion of left female breast
	37208322	Infiltrating ductal carcinoma of axillary tail of left female breast
	37208324	Infiltrating ductal carcinoma of lower inner quadrant of left female breast
	37208325	Infiltrating ductal carcinoma of lower outer quadrant of left female breast
	37208326	Infiltrating ductal carcinoma of axillary tail of right female breast
	37208328	Infiltrating ductal carcinoma of lower inner quadrant of right female breast

	37208329	Infiltrating ductal carcinoma of lower outer quadrant of right female breast
	40486563	Carcinoma of female breast
	40492507	Infiltrating duct carcinoma of female breast
	37018660	Primary malignant inflammatory neoplasm of female breast
	137809	Primary malignant neoplasm of female breast
	3272714	Carcinoma of breast
	3406535	Infiltrating lobular carcinoma of breast
	3662037	Primary malignant neoplasm of breast with axillary lymph node invasion
	4080865	Infiltrating lobular carcinoma of breast
	4112853	Malignant tumor of breast
	4157332	Malignant neoplasm of female breast
	4184597	Paget's disease and intraductal carcinoma of breast
	4220365	Paget's disease and infiltrating duct carcinoma of breast
	4337106	Malignant phyllodes tumor
	35622134	Metaplastic carcinoma of breast
	36536634	Metaplastic carcinoma, NOS, of overlapping lesion of breast
	36541476	Metaplastic carcinoma, NOS, of nipple
	36542964	Lobular carcinoma, NOS, of overlapping lesion of breast
	36547774	Metaplastic carcinoma, NOS, of axillary tail of breast
	36564848	Infiltrating duct carcinoma, NOS, of overlapping lesion of breast
	36716497	Primary invasive pleomorphic lobular carcinoma of breast
	37310457	Locally advanced breast cancer
	44498965	Lobular carcinoma, NOS, of central portion of breast
	44498967	Metaplastic carcinoma, NOS, of upper-outer quadrant of breast
	44499818	Infiltrating duct carcinoma, NOS, of lower-outer quadrant of breast
	44499972	Infiltrating duct carcinoma, NOS, of upper-inner quadrant of breast
	44500419	Lobular carcinoma, NOS, of lower-inner quadrant of breast
	44500599	Infiltrating duct carcinoma, NOS, of nipple
	44500600	Lobular carcinoma, NOS, of upper-outer quadrant of breast
	44500882	Lobular carcinoma, NOS, of nipple
	44501150	Infiltrating duct carcinoma, NOS, of axillary tail of breast
	44501151	Encapsulated papillary carcinoma of central portion of breast
	44501217	Intraductal micropapillary carcinoma of breast, NOS
	44501355	Lobular carcinoma, NOS, of upper-inner quadrant of breast
	44501944	Infiltrating duct carcinoma, NOS, of central portion of breast
	44502039	Metaplastic carcinoma, NOS, of lower-inner quadrant of breast
	44502447	Infiltrating duct carcinoma, NOS, of lower-inner quadrant of breast
	44502449	Metaplastic carcinoma, NOS, of upper-inner quadrant of breast
	44502548	Infiltrating duct carcinoma, NOS, of upper-outer quadrant of breast
	44502958	Lobular carcinoma, NOS, of lower-outer quadrant of breast
	44502959	Lobular carcinoma, NOS, of axillary tail of breast

	44503099	Metaplastic carcinoma, NOS, of lower-outer quadrant of breast
	44503559	Metaplastic carcinoma, NOS, of central portion of breast
	45466558	[M]Paget's disease and intraductal carcinoma of breast
	45547505	Malignant neoplasm: Breast, unspecified
	45766487	Periductal stromal tumor, low grade
Endometrium	4048226	Adenocarcinoma of endometrium
	40491873	Sarcoma of endometrium
	4247238	Primary malignant neoplasm of endometrium
	37115735	Endometrial carcinosarcoma
	37116597	Primary undifferentiated carcinoma of endometrium
	37116596	Primary squamous cell carcinoma of endometrium
	36716616	Primary small cell carcinoma of endometrium
	4110871	Endometrial carcinoma
	36717227	Primary serous adenocarcinoma of endometrium
	36716614	Primary mucinous adenocarcinoma of endometrium
	36716615	Primary mixed adenocarcinoma of endometrium
	37016123	Primary malignant mixed Mullerian neoplasm of endometrium
	37016124	Primary malignant clear cell neoplasm of endometrium
	42538693	Primary endometrioid carcinoma of endometrium of body of uterus
	37016125	Primary adenosquamous carcinoma of endometrium
	4283888	Malignant tumor involving vulva by separate metastasis from endometrium
	4281160	Malignant tumor involving right ovary by separate metastasis from endometrium
	4283877	Malignant tumor involving right fallopian tube by separate metastasis from endometrium
	45486542	Malignant neoplasm of endometrium of corpus uteri
	4095749	Malignant neoplasm of endometrium of corpus uteri
	45419999	Malignant neoplasm of endometrium
Hodgkin Lymphoma	4038835	Hodgkin's disease (clinical)
	42538850	Classical Hodgkin lymphoma
	4195472	Hodgkin lymphoma, nodular sclerosis, grade 2
	4166852	Hodgkin lymphoma, nodular sclerosis, grade 1
	4193008	Hodgkin lymphoma, nodular sclerosis, cellular phase
	4179351	Hodgkin lymphoma, nodular sclerosis
	4322613	Hodgkin lymphoma, nodular lymphocyte predominance
	4216428	Hodgkin lymphoma, mixed cellularity
	4028701	Hodgkin lymphoma, lymphocyte-rich
	4322166	Hodgkin lymphoma, lymphocyte depletion, reticular
	4060382	Hodgkin lymphoma, lymphocyte depletion, diffuse fibrosis
	4028861	Hodgkin lymphoma (category)
	4031667	Hodgkin lymphoma
	45486662	[M]Hodgkin's granuloma

	45513187	[M]Hodgkin's disease, nodular sclerosis, cellular phase
	45466575	[M]Hodgkin's disease, nodular sclerosis NOS
	45439794	[M]Hodgkin's disease, mixed cellularity
	45523129	[M]Hodgkin's disease, lymphocytic predominance
	45493207	[M]Hodgkin's disease, lymphocytic depletion, reticular type
	45480033	[M]Hodgkin's disease, lymphocytic depletion, diffuse fibrosis
	45486663	[M]Hodgkin's disease NOS
	45473314	[M]Hodgkin's disease NOS
	45486661	[M]Hodgkin's disease
	4195472	Hodgkin lymphoma, nodular sclerosis, grade 2
	4166852	Hodgkin lymphoma, nodular sclerosis, grade 1
	4193008	Hodgkin lymphoma, nodular sclerosis, cellular phase
	4179351	Hodgkin lymphoma, nodular sclerosis
	4322613	Hodgkin lymphoma, nodular lymphocyte predominance
	45493207	[M]Hodgkin's disease, lymphocytic depletion, reticular type
	45480033	[M]Hodgkin's disease, lymphocytic depletion, diffuse fibrosis
	45486663	[M]Hodgkin's disease NOS
	45473314	[M]Hodgkin's disease NOS
	45486661	[M]Hodgkin's disease
Non-Hodgkin Lymphoma (excludes Hodgkin concepts)	147411	Follicular non-Hodgkin's lymphoma
	4038838	Non-Hodgkin's lymphoma (clinical)
	4149011	Waldenstrom's macroglobulinemia
	36402787	Waldenstrom macroglobulinemia of blood
	45605307	Undifferentiated (diffuse) non-Hodgkin's lymphoma
	45605307	Undifferentiated (diffuse) non-Hodgkin's lymphoma
	45755330	True histiocytic lymphoma
	45595715	Other specified types of non-Hodgkin lymphoma
	45547547	Other and unspecified types of non-Hodgkin lymphoma
	40491440	Non-Hodgkin's lymphoma of stomach
	4038838	Non-Hodgkin's lymphoma (clinical)
	45590960	Non-Hodgkin lymphoma, unspecified, extranodal and solid organ sites
	45561867	Non-Hodgkin lymphoma, unspecified
	40484012	Non-Hodgkin lymphoma associated with Human immunodeficiency virus infection
	4030288	Non-Hodgkin lymphoma (category)
	45456351	Non-Hodgkin lymphoma
	45571555	Immunoblastic (diffuse) non-Hodgkin's lymphoma
	45426407	HIV disease resulting in other types of non-Hodgkin lymphoma
	45556932	HIV disease resulting in other types of non-Hodgkin lymphoma
	4002357	Follicular non-Hodgkin's lymphoma, small cleaved cell (clinical)
	4001329	Follicular non-Hodgkin's lymphoma, mixed small cleaved cell and large cell (clinical)

	4003833	Follicular non-Hodgkin's lymphoma, large cell (clinical)
	40492018	Follicular non-Hodgkin's lymphoma of skin
	4147411	Follicular non-Hodgkin's lymphoma
	4003831	Diffuse non-Hodgkin's lymphoma, undifferentiated
	4002356	Diffuse non-Hodgkin's lymphoma, small cell (clinical)
	4001328	Diffuse non-Hodgkin's lymphoma, lymphoblastic (clinical)
	4003832	Diffuse non-Hodgkin's lymphoma, immunoblastic (clinical)
	4003830	Diffuse non-Hodgkin's lymphoma
Lymphoma	4147411	Follicular non-Hodgkin's lymphoma
	4038838	Non-Hodgkin's lymphoma (clinical)
	432571	Malignant lymphoma
	35624275	Primary bone lymphoma
	373152	Primary central nervous system lymphoma
	4002358	Lymphoepithelioid lymphoma (clinical)
	4174442	Lymphoma of intestine
	434592	B-cell lymphoma (clinical)
	434881	Peripheral T-cell lymphoma (clinical)
	920120	Blastic NK-cell lymphoma
	1567674	Malignant immunoproliferative diseases and certain other B-cell lymphomas
	4001328	Diffuse non-Hodgkin's lymphoma, lymphoblastic (clinical)
	4001329	Follicular non-Hodgkin's lymphoma, mixed small cleaved cell and large cell (clinical)
	4002356	Diffuse non-Hodgkin's lymphoma, small cell (clinical)
	4002357	Follicular non-Hodgkin's lymphoma, small cleaved cell (clinical)
	4003830	Diffuse non-Hodgkin's lymphoma
	4003833	Follicular non-Hodgkin's lymphoma, large cell (clinical)
	4029188	Primary cutaneous CD30+ large T-cell lymphoma
	4038839	Hodgkin lymphoma, nodular lymphocyte predominance (clinical)
	4038841	Lymphocyte-rich classical Hodgkin lymphoma
	4041800	Burkitt's lymphoma (clinical)
	4082487	Cutaneous/peripheral T-cell lymphoma
	4082627	Enteropathy-associated T-cell lymphoma
	4093298	HIV disease resulting in other types of non-Hodgkin's lymphoma
	4147822	Lymphoma stage I
	4150201	Lymphomatoid papulosis
	4184976	Angioimmunoblastic T-cell lymphoma
	4210767	Lymphoma stage III
	4212994	Extranodal NK/T-cell lymphoma, nasal type
	4283505	Lymphoma stage IV
	4287493	Lymphoma involves spleen
	4299149	Anaplastic large T-cell systemic malignant lymphoma
	4300704	Diffuse large B-cell lymphoma (nodal/systemic with skin involvement)

	4301666	Subcutaneous panniculitis-like T-cell lymphoma
	4301668	Primary cutaneous follicular center B-cell lymphoma
	36402787	Waldenstrom macroglobulinemia of blood
	36531651	Precursor T-cell lymphoblastic lymphoma of intra-abdominal lymph nodes
	37017595	Burkitt lymphoma co-occurrent with human immunodeficiency virus infection
	37397538	Primary pulmonary lymphoma
	40481522	Primary mediastinal (thymic) large B-cell lymphoma
	40481901	Mantle cell lymphoma
	40482893	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma)
	40483374	Hepatosplenic T-cell lymphoma
	40484012	Non-Hodgkin lymphoma associated with Human immunodeficiency virus infection
	40486171	Diffuse follicle center lymphoma
	40488896	Anaplastic large cell lymphoma, ALK negative
	42538056	Anaplastic lymphoma kinase positive anaplastic large cell lymphoma
	44498995	Malignant lymphoma, small B lymphocytic, NOS, of lymph node, NOS
	44499005	Precursor T-cell lymphoblastic lymphoma of lymph node, NOS
	45425416	Lymphoma stage III
	45426407	HIV disease resulting in other types of non-Hodgkin lymphoma
	45428745	Lymphoma stage II
	45445303	Lymphoma stage I
	45448592	Lymphoma stage IV
	45453022	Blastic NK-cell lymphoma
	45456351	Non-Hodgkin lymphoma
	45463164	Anaplastic large cell lymphoma, ALK-positive
	45479949	Lymphoid and histiocytic malignancy NOS
	45487194	Lymphomatoid papulosis
	45547547	Other and unspecified types of non-Hodgkin lymphoma
	45556932	HIV disease resulting in other types of non-Hodgkin lymphoma
	45561857	Other mature T/NK-cell lymphomas
	45561867	Non-Hodgkin lymphoma, unspecified
	45566646	Blastic NK-cell lymphoma
	45571555	Immunoblastic (diffuse) non-Hodgkin's lymphoma
	45581942	Lymphomatoid papulosis
	45590960	Non-Hodgkin lymphoma, unspecified, extranodal and solid organ sites
	45595711	Mature T/NK-cell lymphoma, unspecified
	45595715	Other specified types of non-Hodgkin lymphoma
	45605307	Undifferentiated (diffuse) non-Hodgkin's lymphoma
	45755330	True histiocytic lymphoma
	45755343	Mixed small and large cell (diffuse) non-Hodgkin's lymphoma

Appendix I. Table 2. List of concept sets used to identify conditions included in the frailty score.

Condition	Concept ID	Concept Name
Mobility and transfer problems	4053076	Mobility poor
	4306934	Impaired mobility
	4052049	Mobility fair
	4310235	Reduced mobility
	4031883	Impaired bed mobility
	4032531	Impaired wheelchair mobility
	4052047	Mobility very poor
	4119464	Does not transfer between wheelchair and toilet
	4118805	Unable to transfer between wheelchair and toilet
	4199114	Difficulty mobilizing using mobility aids
	4199113	Does not mobilize using mobility aids
	4199111	Unable to mobilize using mobility aids
	4023190	Wheelchair bound
	4136754	Dependent on helper pushing wheelchair
	4200353	Able to mobilize using mobility aids
	4199115	Able to mobilize using wheelchair
	4199721	Able to move around supporting self on furniture
	44790310	Able to walk short distances
	45878557	Completely immobile
	36716239	Dependent for sitting
	36716240	Dependent for standing
	4146424	Dependent for walking
	46272933	Deterioration in ability to walk
	4200194	Difficulty mobilizing
	4199094	Difficulty mobilizing indoors
	4199114	Difficulty mobilizing using mobility aids
	4199116	Difficulty mobilizing using wheelchair
	4199431	Difficulty moving
	4200817	Difficulty moving around supporting self on furniture
	4107789	Difficulty shuffling
	4107851	Difficulty sitting
	4199552	Difficulty sitting unsupported
	4093668	Difficulty standing

	4154006	Difficulty transferring weight
	36714126	Difficulty walking
	4086550	Difficulty walking up a slope
	4112788	Difficulty weight-bearing
	4199112	Does mobilize using aids
	4199725	Does mobilize using wheelchair
	4200815	Does move around supporting self on furniture
	4200193	Does not mobilize
	4200798	Does not mobilize indoors
	4200183	Does not move
	4084746	Does not shuffle
	4106333	Does not sit
	4199551	Does not sit unsupported
	4106335	Does not stand
	4154005	Does not transfer weight
	4086871	Does not walk
	4086549	Does not walk up a slope
	4112787	Does not weight-bear
	4295037	Get up and go test - abnormal
	4009877	Immobile
	1621081	Immobile or
	4031883	Impaired bed mobility
	4306934	Impaired mobility
	3198828	Increased weakness when ambulating
	4010359	Loss of control of walking
	1314392	Patient is not ambulatory, bed ridden, immobile, confined to chair, wheelchair bound, dependent on helper pushing wheelchair, independent in wheelchair or minimal help in wheelchair
	1314394	Patient not ambulatory, bed ridden, immobile, confined to chair, wheelchair bound, dependent on helper pushing wheelchair, independent in wheelchair or minimal help in wheelchair
	44790681	Patient unable to get up unaided
	4012646	Stick only for walking
	4012944	Tripod/quadrupod: walking
	4199550	Unable to mobilize
	4199093	Unable to mobilize indoors
	4199111	Unable to mobilize using mobility aids

	4200355	Unable to mobilize using wheelchair
	4200350	Unable to move around supporting self on furniture
	4105451	Unable to shuffle
	4106332	Unable to sit
	4023187	Unable to sit unsupported
	4060223	Unable to stand
	4151066	Unable to transfer weight
	4086548	Unable to walk
	44792042	Unable to walk long distances
	4086874	Unable to walk up a slope
	4116707	Unable to weight-bear
	44789400	Uses wheelchair outdoors
	4012945	Uses zimmer frame
	45878235	Very limited, Immobile
	4266144	Walking aid use - finding
	439405	Walking disability
	4240470	wheelchair
	4086557	Difficulty walking up stairs
	4200822	Difficulty managing stairs
	4022073	Dependence on wheelchair
Housebound	40299189	Housebound
	4052962	Housebound
	45877743	Bedridden
	4022076	Patient dependence on care provider
	4019828	Personal care assistance at home (procedure)
	4022523	General home assistance of patient
Activity limitation	44811145	Unfit for activity
	5767124	Difficulty performing personal grooming activity
	36716238	Dependent for personal hygiene activity
	4110470	Difficulty performing personal hygiene activity
	4109859	Unable to perform bathing activity
	4032520	Activity of daily living (ADL) alteration
	4031882	Activity alteration
	4137049	Disability affecting daily living
	4030753	Physical functional dependency (finding)
	36713755	Functionally dependent
Visual impairment	4265433	Visual impairment

	4023310	Blindness AND/OR vision impairment level (disorder)
	40305578	Blindness
	44797518	Visual disturbances and blindness
	375545	cataract
	37541	Glaucoma
	374034	Visual disturbance
	42872584	Registration of visual impairment
Hearing impairment	36715579	Acquired hearing loss
	377889	Hearing loss
	439378	Ear anomalies with hearing impairment
	444291	Sensory hearing loss
	44805060	Wears bone anchored hearing aid
	379832	Mixed conductive AND sensorineural hearing loss
	378444	Hearing disroder
	42539697	External hearing aid in situ
	4246497	Hearing aid
Requirement for care	4192880	Lives in a residential home
	35609081	Home visit requested by care home staff
	4052486	Lives in a nursing home
	4192880	Lives in a residential home
	44791364	Lives in care home
	4074789	Lives in supported home
	4022081	Living in residential institution
	3661927	Living temporarily in care home
	44790305	Local authority care home
	40486978	Nursing home acquired pressure ulcer
	44790706	Pain commenced - residential home
	44791204	Place of occurrence of injury: residential home environment
	44802299	Previously lived in care home
	44788859	Private or voluntary care home
	4147552	Private residential home
	765265	Problem related to living in residential institution
	36713971	Referred by care home
	44814152	Referred by nursing home
	44814153	Referred by residential home
	4119866	Residential home

	44804659	Residential home acquired pressure ulcer
	4305680	Residential institution
	37310422	Seen by clinical pharmacist in care home
	4088536	Seen in nursing home
	44788849	Provision of residential care (regime/therapy)
	37108723	Assisted living facility patient
	44807727	Has a paid carer
	42535090	Need for personal care assistance
	4081589	Has a caregiver
Social vulnerability	4019836	Social exclusion
	4228687	Impaired social interaction
	4309238	Social isolation
	4019835	Social withdrawal
	4297462	Social isolation (rejection)
	4172829	Limited social contact
	4317527	Family-related social factor
	42690410	Carer behavior is cause for safeguarding concern
	44792191	Extensive support provided by carer
	4147192	Feeling lonely
	44805255	Has an informal carer
	44805672	Has an older carer
	44807727	Has a paid carer
	44805674	Has a parent carer
	37394063	Has kinship carer
	44813864	Has socially isolated carer
	44806914	Has voluntary carer
	44792192	Inadequate support provided by carer
	4023168	Lives alone
	4052158	Lives alone needs housekeeper
	4053087	Lives alone no help available
	45879223	Lonely
	44789099	Parent is informal carer
	44789487	Partner is informal carer
	44810043	Referred by Social Services
	44790469	Relative is informal carer
	44789986	Report received from social services
	37208707	Requires carer to be present at encounters
	4052789	Social problem

	4209159	Social problem not due to a mental disorder
	44788883	Under care of social services
	4221049	Vulnerable adult
	44791055	Vulnerable elderly person
	44791931	Vulnerable family
	4151777	Vulnerable family support
	44803964	Vulnerable group
	4116985	Vulnerable personality
Falls	4087528	Recurrent falls
	4256754	Falls caused by medication
	4224116	Unexplained recurrent falls
	4329906	At risk for injury due to fall
	436583	Fall (observation)
	435991	accidental fall
	4184243	Elderly fall
	4323345	History of fall
Urinary incontinence	193326	Urge incontinence of urine
	193598	Extravasation of urine
	193874	Nocturnal enuresis
	195007	Female stress incontinence
	195079	Functional urinary incontinence
	197102	Unaware of passing urine
	197378	Overflow incontinence of urine
	197672	Urinary incontinence
	443524	Mixed urinary incontinence
	444035	Incontinence
	606405	Extra urethral urinary incontinence
	606955	Stress incontinence following surgical procedure
	4012368	Increased frequency of urination
	4030763	At risk for urge incontinence
	4032498	Abnormal bladder continence
	4032530	Total urinary incontinence
	4092642	Urinary loss
	4096552	Unaware of need to urinate
	4126278	Postural urinary incontinence
	4153667	Urinary incontinence due to urethral sphincter incompetence
	4172646	Urinary incontinence of non-organic origin

	4302457	Double incontinence
	4314023	Incontinence due to detrusor instability
	37119132	Urinary incontinence co-occurrent and due to prolapse of female genital organ
	37208161	Daily urinary incontinence
	40480232	Male urinary stress incontinence
	40481801	Stress incontinence after prostatectomy
	40490423	Incontinence without sensory awareness
	42536555	Stress incontinence co-occurrent and due to pelvic organ prolapse
	42538537	Overflow incontinence of urine due to prolapse of female genital organ
	42538538	Urge incontinence due to prolapse of female genital organ
	42538539	Mixed incontinence due to prolapse of female genital organ
	42872846	Intermittent urinary incontinence
	44808460	Sneezing incontinence of urine
	45757352	Urinary incontinence due to benign prostatic hypertrophy
	45770268	Functional urinary and faecal incontinence
Weight loss and anorexia	436675	Anorexia nervosa
	4091029	Anorexia symptom
	435928	Abnormal weight loss
	4216971	Mood anorexia
	4333683	Atypical anorexia nervosa
	4300305	Anorexia nervosa, restricting type
	44784528	Anorexia nervosa in remission
	4269485	Anorexia nervosa, binge-eating purging type
	37204325	Facial dysmorphism, anorexia, cachexia, eye and skin anomalies syndrome
	442165	Loss of appetite
	44788734	Complaining of weight loss
	4156515	Malnutrition (calorie)
	763515	Chronic disease-related malnutrition
	45773690	Hypoalbuminemia due to protein calorie malnutrition
	134765	Cachexia

	4109384	Cardiac cachexia
	4347292	Muscle cachexia
	37312021	Malignant cachexia
	36676905	Severe dermatitis, multiple allergies, metabolic wasting syndrome
	4078430	Severe systemic illness-induced respiratory muscle wasting
	4031171	Severe systemic illness-induced skeletal muscle wasting
	4031170	Severe systemic illness tissue wasting
	4123542	Wasting disease
	4229881	Weight loss
Memory and cognitive problems	439795	Minimal cognitive impairment
	443432	Impaired cognition
	761978	Cognitive impairment due to multiple sclerosis
	3654469	Amnestic mild cognitive disorder
	3654907	Cognitive impairment caused by ingestible alcohol
	4009705	Age-related cognitive decline
	4022572	Disturbance of cognitive learning
	4023989	Cognitive perceptual pattern
	4047110	Language-related cognitive disorder
	4297400	Mild cognitive disorder
	4333671	Age-associated memory impairment
	40480615	Cognitive disorder
	40482301	Residual cognitive deficit as late effect of cerebrovascular accident
	42535016	Cognitive deficit in communication skills
	42535017	Cognitive deficit in visuospatial function
	42535018	Cognitive deficit in psychomotor function
	42535681	Cognitive deficit due to and following ischaemic cerebrovascular accident
	42535682	Cognitive deficit due to and following hemorrhagic cerebrovascular accident
	42535706	Cognitive deficit due to and following embolic cerebrovascular accident
	42537139	Dissociative neurological symptom disorder co-occurrent with cognitive symptoms

	42539256	Cognitive deficit due to and following cerebrovascular disease
	42539270	Cognitive deficit due to and following nontraumatic subarachnoid hemorrhage
	42539271	Cognitive deficit due to and following nontraumatic intracerebral hemorrhage
	45765899	Moderate cognitive impairment
	45765900	Severe cognitive impairment
	46271045	Neurocognitive disorder
	40480615	Cognitive disorder
	4182210	Dementia
	42690615	Difficulty remembering past events
	42689981	Difficulty remembering people
	42689830	Difficulty remembering places
	42689982	Difficulty remembering routines
	42690112	Does not remember past events
	42690742	Does not remember people
	42690113	Does not remember places
	42689849	Does not remember routines
	443432	Impaired cognition
	4103572	Organic memory impairment
	4135668	Poor auditory sequential memory
	4085496	Poor long-term memory
	4084412	Poor short-term memory
	4131380	Poor visual sequential memory
	42690368	Unable to remember past events
	42690369	Unable to remember people
	42690647	Unable to remember places
	42690370	Unable to remember routines
	4141586	Uncompensated short term memory deficit
	4043378	Frontotemporal dementia
Dyspnoea	4144682	Expiratory Dyspnoea
	4192279	Medical Research Council Dyspnoea scale grade 5
	4193263	Medical Research Council Dyspnoea scale grade 2
	4206307	Paroxysmal nocturnal Dyspnoea
	4212233	Dyspnoea after eating

	4217021	Dyspnoea, class II
	4219335	Dyspnoea, class III
	4219740	Borg Breathlessness Score finding
	4228754	Dyspnoea associated with AIDS
	4244276	Paroxysmal Dyspnoea
	4248284	Dyspnoea, class IV
	4263848	Dyspnoea on exertion
	4307188	Medical Research Council Dyspnoea scale grade 3
	4310172	Medical Research Council Dyspnoea scale grade 4
	35610140	eMRC (extended Medical Research Council) dyspnoea scale grade 2
	35610141	eMRC (extended Medical Research Council) dyspnoea scale grade 3
	35610142	eMRC (extended Medical Research Council) dyspnoea scale grade 5a
	35610143	eMRC (extended Medical Research Council) dyspnoea scale grade 4
	35610144	eMRC (extended Medical Research Council) dyspnoea scale grade 5b
	36685569	mMRC (modified Medical Research Council) dyspnoea scale grade 2
	36685570	mMRC (modified Medical Research Council) dyspnoea scale grade 3
	36685571	mMRC (modified Medical Research Council) dyspnoea scale grade 4
	312437	Dyspnoea
Sleep disturbance	435657	Dyssomnia
	4204989	Disturbance in sleep behavior
	40480927	Sleep dysfunction with sleep stage disturbance
	40482260	Sleep dysfunction with arousal disturbance
	4132137	Sleep pattern disturbance
	435524	Sleep disorder
	42690122	Does not sleep
	374905	Non-organic sleep disorder
	443544	Organic sleep disorder
	4200883	Poor sleep pattern
	4215402	Primary insomnia

	37110488	Chronic insomnia
	4102985	Nonorganic insomnia
	4086851	Cannot sleep at all
	4115402	Difficulty sleeping
	42689992	Difficulty sleeping without sedation
	42689991	Difficulty sleeping with sedation
	43530738	Disruptions of 24 hour sleep-wake cycle
	4204989	Disturbance in sleep behavior
	42690122	Does not sleep
	42690715	Does not sleep without sedation
	42690123	Does not sleep with sedation
	434172	Insomnia with sleep apnea
	436522	Irregular sleep-wake pattern
	3173994	Poor sleep hygiene
	4305303	Sleep deprivation
	42690380	Unable to sleep without sedation
	42690379	Unable to sleep with sedation
Anaemia and haematinic deficiency	434622	deficiency anaemias
	4306430	Ferritin level low
	37016158	Low serum ferritin
	136949	Refractory anaemia with excess blasts (clinical)
	137829	Aplastic anaemia
	140065	Pure red cell aplasia
	140681	Constitutional aplastic anaemia
	432282	Sideroblastic anaemia
	432295	Pernicious anaemia
	432588	Megaloblastic anaemia due to vitamin B-12 deficiency
	432875	Anaemia due to chronic blood loss
	433168	Iron deficiency anaemia secondary to inadequate dietary iron intake
	434894	Acute posthemorrhagic anaemia
	435503	Hemolytic anaemia
	435789	Megaloblastic anaemia
	436659	Iron deficiency anaemia
	437247	Anaemia of chronic disease
	437834	Non-autoimmune hemolytic anaemia

	438722	Non megaloblastic anaemia associated with nutritional deficiency
	439777	Anaemia
	440977	Megaloblastic anaemia due to folate deficiency
	440979	Acquired hemolytic anaemia
	441258	Anaemia in neoplastic disease
	441269	Autoimmune hemolytic anaemia
	443961	Anaemia of chronic renal failure
	602143	Anaemia due to chronic kidney disease stage 1
	603007	Pernicious anaemia due to autoimmune disorder
	603011	Vitamin B12 deficiency anaemia following total gastrectomy
	605330	Restless leg syndrome due to iron deficiency anaemia
	606065	Congenital megaloblastic anaemia due to transcobalamin II deficiency
	606921	Post gastrectomy iron deficiency anaemia
	606928	Iron deficiency anaemia due to celiac disease
	606940	Drug-induced non autoimmune hemolytic anaemia
	607426	Vitamin B12 deficiency anaemia due to chronic atrophic gastritis
	608596	Anaemia caused by antineoplastic agent
	3661626	Megaloblastic anaemia due to dihydrofolate reductase deficiency
	4002495	Refractory anaemia with excess blasts in transformation (clinical)
	4003185	Refractory anaemia (clinical)
	4003186	Refractory anaemia with ringed sideroblasts (clinical)
	4006467	Anaemia due to infection
	4006468	Anaemia due to physical agent
	4008273	Coombs negative hemolytic anaemia
	4008663	Megaloblastic anaemia due to exfoliative dermatitis
	4009306	Anaemia due to copper deficiency
	4009785	Anaemia due to membrane defect
	4015896	Anaemia due to niacin deficiency
	4019001	Regenerative anaemia
	4021911	Megaloblastic anaemia due to poor nutrition
	4031699	Humoral immunologic aplastic anaemia
	4032006	Dimorphic anaemia

	4032352	Hemolytic anaemia due to hyperbaric oxygen
	4034963	Megaloblastic anaemia, thiamine-responsive, with diabetes mellitus and sensorineural deafness
	4035974	Drug-induced enzyme deficiency anaemia
	4039536	Autoimmune hemolytic anaemia due to complement
	4044728	Thiamine-responsive megaloblastic anaemia
	4045142	Megaloblastic anaemia due to gastrectomy
	4046563	G-6-PD class I variant anaemia
	4071444	Anaemia of thyroid dysfunction
	4079181	G-6-PD class III variant anaemia
	4082253	Unstable hemoglobin disease
	4082917	Drug-induced immune hemolytic anaemia, immune complex type
	4085853	Hemolytic anaemia due to babesiosis
	4092893	Anaemia due to vitamin E deficiency
	4096927	Megaloblastic anaemia due to vitamin B-12 malabsorption with proteinuria
	4097961	Acute megaloblastic anaemia due to dialysis
	4098008	Folate deficiency anaemia due to malabsorption
	4098009	Folate deficiency anaemia due to liver disorders
	4098013	Hemolytic anaemia due to hexokinase deficiency
	4098017	Primary cold-type hemolytic anaemia
	4098018	Mechanical hemolytic anaemia
	4098019	Toxic hemolytic anaemia
	4098027	Aplastic anaemia due to radiation
	4098131	Myelophthisic anaemia
	4098145	Idiopathic aplastic anaemia
	4098627	Idiopathic hypochromic anaemia
	4098740	Vitamin B12 deficiency anaemia due to malabsorption with proteinuria
	4098746	Hemolytic anaemia due to pyruvate kinase deficiency
	4098747	Anaemia due to disorders of nucleotide metabolism
	4098760	Transient hypoplastic anaemia
	4098762	Pyridoxine-responsive sideroblastic anaemia
	4099508	Refractory anaemia without sideroblasts, so stated
	4099603	Megaloblastic anaemia due to hemodialysis

	4100962	Megaloblastic anaemia due to impaired absorption of folate
	4100985	Iron deficiency anaemia due to dietary causes
	4100987	Folate deficiency anaemia, drug-induced
	4100991	Hemolytic anaemia due to triose phosphate isomerase deficiency
	4100998	Aplastic anaemia due to toxic cause
	4101000	Secondary sideroblastic anaemia due to drugs and toxins
	4101001	Chronic anaemia
	4101458	Combined B12 and folate deficiency anaemia
	4101573	Vitamin C deficiency anaemia
	4101582	Aplastic anaemia due to chronic disease
	4101583	Aplastic anaemia due to infection
	4101584	Secondary sideroblastic anaemia due to disease
	4104541	Anaemia due to pentose phosphate pathway defect
	4105643	Myasthenic syndrome due to pernicious anaemia
	4114026	Normocytic anaemia
	4116343	Normocytic anaemia following acute bleed
	4120446	Iron deficiency without anaemia
	4120448	Normocytic anaemia due to aplasia
	4120450	Normocytic anaemia due to chronic blood loss
	4121106	Microcytic anaemia
	4121110	Selective malabsorption of cyanocobalamin
	4121115	Sickle cell anaemia with high hemoglobin F
	4122079	Deficiency anaemias, excluding iron
	4122923	Dilutional anaemia
	4122924	Anaemia of renal disease
	4122927	Combined deficiency anaemia
	4125491	Megaloblastic anaemia due to dietary causes
	4125493	Vegan's anaemia
	4125630	Chronic non-spherocytic hemolytic anaemia
	4130191	Secondary warm autoimmune hemolytic anaemia
	4130680	Autoimmune hemolytic anaemia, categorised by antibody class AND/OR complement
	4131127	Secondary autoimmune hemolytic anaemia
	4131914	Sickle cell anaemia with coexistent alpha-thalassemia
	4131915	Primary (idiopathic) autoimmune hemolytic anaemia

	4131917	Paroxysmal cold hemoglobinuria
	4131919	Drug-induced immune hemolytic anaemia, hapten type
	4132085	Anaemia due to alloimmune destruction of transfused red cells
	4135931	Anaemia of endocrine disorder
	4143167	Autoimmune hemolytic anaemia due to IgA plus complement
	4143351	Folate deficiency anaemia due to dietary causes
	4143629	Anaemia due to mechanical damage
	4144077	G-6-PD class II variant anaemia
	4144811	Anaemia due to zinc deficiency
	4145277	HNSHA due to pyrimidine-5'-nucleotidase deficiency
	4146086	Constitutional aplastic anaemia with malformation
	4146088	Aplastic anaemia due to drugs
	4146771	Anaemia in ovarian carcinoma
	4146936	Drug-induced autoimmune hemolytic anaemia
	4147365	Anaemia of adrenal dysfunction
	4147491	Vitamin B12 deficiency anaemia due to dietary causes
	4147600	Megaloblastic anaemia due to pancreatic insufficiency
	4147911	Megaloblastic anaemia due to inborn errors of metabolism
	4148471	Fanconi's anaemia
	4149183	Megaloblastic anaemia due to error of folate metabolism
	4150499	Refractory megaloblastic anaemia
	4150547	Anaemia secondary to renal failure
	4151502	Hemolytic anaemia due to Clostridium welchii
	4155187	Traumatic cardiac hemolytic anaemia
	4156842	Intracorpuscular hemolytic anaemia
	4157495	Sideropenic anaemia with reticuloendothelial siderosis
	4158891	Anaemia due to isoimmunization
	4159651	Traumatic hemolytic anaemia
	4159748	Hand-foot syndrome in sickle cell anaemia
	4160238	Simple chronic anaemia

	4160887	Cold autoimmune hemolytic anaemia
	4168286	Anaemia due to starvation
	4168772	Megaloblastic anaemia due to chronic hemolytic anaemia
	4171026	HNSHA due to NADH diaphorase deficiency
	4172446	Microcytic normochromic anaemia
	4173028	Idiopathic sideroblastic anaemia
	4174412	Anaemia due to copper
	4176884	Hemolytic anaemia due to nonlymphoid neoplasm
	4177177	Cellular immunologic aplastic anaemia
	4178677	Congenital nonspherocytic hemolytic anaemia due to inborn error of metabolism
	4184200	Secondary aplastic anaemia
	4184603	Megaloblastic anaemia due to Zollinger-Ellison syndrome
	4184758	Acquired aplastic anaemia
	4195171	Normocytic hypochromic anaemia
	4195271	Megaloblastic anaemia due to vegetarianism
	4201444	Anaemia due to riboflavin deficiency
	4203291	HNSHA due to increased adenosine deaminase activity
	4207240	Anaemia due to intrinsic red cell abnormality
	4211348	Aplastic anaemia associated with pancreatitis
	4211695	Acute pure red cell aplasia
	4213893	Achlorhydric anaemia
	4214023	G-6-PD class V variant anaemia
	4215784	Autoimmune hemolytic anaemia due to IgM
	4215791	Acute megaloblastic anaemia secondary to total parenteral nutrition
	4216915	Hemoglobin S sickling disorder with crisis
	4217370	Aase syndrome
	4218100	Hemolytic anaemia due to drugs
	4218974	Hypoplastic anaemia
	4219253	Anaemia due to arsenic hydride
	4219359	G-6-PD class IV variant anaemia
	4219853	Warm autoimmune hemolytic anaemia
	4220697	Acute megaloblastic anaemia
	4221567	Megaloblastic anaemia due to disease of small intestine

	4223031	Anaemia associated with AIDS
	4223896	Mycoplasmal anaemia
	4225810	Aplastic anaemia associated with AIDS
	4228194	Congenital hypoplastic anaemia
	4228444	Acquired hemolytic anaemia associated with AIDS
	4231887	Secondary acquired sideroblastic anaemia
	4234973	Chronic acquired pure red cell aplasia
	4235788	Familial megaloblastic anaemia
	4238904	Autoimmune hemolytic anaemia due to IgA
	4241982	Congenital dyserythropoietic anaemia, type I
	4242111	HNSHA due to phosphoglycerate kinase deficiency
	4243831	Anaemia of pituitary deficiency
	4243950	Megaloblastic anaemia due to blind loop syndrome
	4244129	Anaemia due to decreased red cell production
	4246105	Hemolytic anaemia with emphysema AND cutis laxa
	4247416	Megaloblastic anaemia due to congenital deficiency of intrinsic factor
	4250028	Acute megaloblastic anaemia due to nitrous oxide
	4254249	HNSHA due to pyruvate kinase deficiency
	4254380	Coombs positive hemolytic anaemia
	4258685	HNSHA due to triosephosphate isomerase deficiency
	4260689	Anaemia due to multiple mechanisms
	4261354	Megaloblastic anaemia due to decreased intake of vitamin B-12
	4262948	Microcytic hypochromic anaemia
	4263315	Normocytic normochromic anaemia
	4264046	Sickle cell-hemoglobin E disease
	4265915	HNSHA due to diphosphoglycerate mutase deficiency
	4268894	Acute megaloblastic anaemia due to severe illness
	4269764	Glucose-6-phosphate dehydrogenase deficiency anaemia
	4269919	Autoimmune hemolytic anaemia due to IgG plus complement
	4271197	Idiopathic paroxysmal cold hemoglobinuria
	4278920	Anaemia due to lead
	4280070	Antibody-mediated anaemia
	4280354	Nutritional anaemia

	4282785	Megaloblastic anaemia due to nontropical sprue
	4284415	Megaloblastic anaemia due to increased requirements
	4286660	Congenital dyserythropoietic anaemia, type II
	4287402	Anaemia of parathyroid dysfunction
	4287574	Megaloblastic anaemia due to error of cobalamin metabolism
	4291002	Megaloblastic anaemia due to drugs
	4297024	Hemolytic anaemia due to Bartonella
	4297537	Hemolytic anaemia due to infection
	4298690	Immunologic aplastic anaemia
	4298975	Hemolytic anaemia due to malaria
	4300295	Drug-induced sideroblastic anaemia
	4303199	Anaemia due to pantothenic deficiency
	4306199	Perinatal anaemia
	4307469	Sports anaemia
	4307799	Anaemia due to diabetes mellitus
	4308062	Diaphyseal dysplasia with anaemia
	4308125	Macrocytic anaemia
	4311676	Anaemia due to vitamin A deficiency
	4312008	Anaemia due to substance
	4312853	Anaemia due to vitamin B-6 deficiency
	4313413	Anaemia due to chlorate
	4313581	Hapten type high affinity hemolytic anaemia
	4314111	Non megaloblastic anaemia due to alcoholism
	4318674	Chronic idiopathic autoimmune hemolytic anaemia
	4319914	Anaemia due to radiation
	4323223	Anaemia due to medication
	4329173	Anaemia of gonadal dysfunction
	4330322	Anaemia due to disturbance of proliferation AND/OR differentiation of hematopoietic stem cells
	4336555	G-6-PD variant enzyme deficiency anaemia
	4338370	Megaloblastic anaemia due to alcoholism
	4338976	Megaloblastic anaemia due to tropical sprue
	35624317	Hemolytic anaemia due to adenylate kinase deficiency
	35624756	Anaemia due to and following chemotherapy
	36680584	Autosomal dominant aplasia and myelodysplasia
	36713571	Megaloblastic anaemia due to vitamin B12 deficiency secondary to intestinal disease

	36713572	Vitamin B12 deficiency anaemia caused by drug
	36713573	Acquired iron deficiency anaemia due to increased iron requirement
	36713763	Autoimmune hemolytic anaemia mixed type
	36715009	Adult-onset autosomal recessive sideroblastic anaemia
	36715492	Megaloblastic anaemia due to folate deficiency due to increased requirement
	36715580	Acquired thiamine deficiency anaemia
	36715584	Refractory anaemia with ringed sideroblasts associated with marked thrombocytosis
	36716029	Hyperuricemia, anaemia, renal failure syndrome
	36716126	Iron-refractory iron deficiency anaemia
	36716259	Pancreatic insufficiency, dyserythropoietic anaemia, calvarial hyperostosis syndrome
	36716460	X-linked congenital dyserythropoietic anaemia with thrombocytopenia
	37016121	Anaemia following acute postoperative blood loss
	37016151	Aplastic anaemia caused by antineoplastic agent
	37017132	Anaemia co-occurrent with human immunodeficiency virus infection
	37017165	GATA binding protein 1 related thrombocytopenia with dyserythropoiesis
	37017285	Acquired hemolytic anaemia co-occurrent with human immunodeficiency virus infection
	37018722	Anaemia caused by zidovudine
	37019055	Aplastic anaemia co-occurrent with human immunodeficiency virus infection
	37019193	Anaemia co-occurrent and due to chronic kidney disease stage 3
	37110070	Mitochondrial myopathy with sideroblastic anaemia syndrome
	37110336	Acquired iron deficiency anaemia due to decreased absorption
	37110727	Nonspherocytic hemolytic anaemia due to deficiency of adenosinetriphosphatase
	37110923	Severe congenital hypochromic anaemia with ringed sideroblasts
	37111627	Central nervous system calcification, deafness, tubular acidosis, anaemia syndrome

	37116297	Secondary autoimmune hemolytic anaemia co-occurrent and due to chronic inflammatory disease
	37116298	Secondary autoimmune hemolytic anaemia co-occurrent and due to lymphoproliferative disorder
	37116300	Secondary autoimmune hemolytic anaemia co-occurrent and due to rheumatic disorder
	37116301	Secondary autoimmune hemolytic anaemia co-occurrent and due to ulcerative colitis
	37117740	Secondary autoimmune hemolytic anaemia co-occurrent and due to systemic lupus erythematosus
	37119138	Iron deficiency anaemia due to blood loss
	37204236	X-linked dyserythropoietic anaemia with abnormal platelets and neutropenia
	37204287	Hemoglobinopathy Toms River
	37204551	Hereditary isolated aplastic anaemia
	37312032	Anaemia due to chronic infectious disease
	37395652	Anaemia in chronic kidney disease stage 5
	37397036	Autosomal recessive sideroblastic anaemia
	37398911	Anaemia in chronic kidney disease stage 4
	40478891	Erythropoietin resistance in anaemia of chronic kidney disease
	40599994	X chromosome-linked sideroblastic anaemia
	42536530	Hereditary vitamin B12 deficiency anaemia
	42536531	Hereditary folate deficiency anaemia
	42537687	Anaemia due to metabolic disorder
	42872405	Anaemia, pre-end stage renal disease on erythropoietin protocol
	44783626	Pulmonary arterial hypertension associated with chronic hemolytic anaemia
	44806268	Refractory anaemia with multilineage dysplasia
	44810002	Recurrent anaemia
	45768812	Anaemia in chronic kidney disease
	45768813	Anaemia in end stage renal disease
	45768941	Chronic hemolytic anaemia
	45773534	Anaemia in malignant neoplastic disease
	46272744	Hypochromic microcytic anaemia with iron overload
Hypertension	312648	Benign essential hypertension
	4215640	Benign essential hypertension complicating AND/OR reason for care during childbirth

	4034031	Benign essential hypertension complicating AND/OR reason for care during pregnancy
	4148205	Benign essential hypertension complicating AND/OR reason for care during puerperium
	4269358	Benign essential hypertension in obstetric context
	320128	Essential hypertension
	4083723	Essential hypertension complicating AND/OR reason for care during childbirth
	4302591	Essential hypertension complicating AND/OR reason for care during pregnancy
	4321603	Essential hypertension complicating AND/OR reason for care during puerperium
	4217486	Essential hypertension in obstetric context
	4058987	High-renin essential hypertension
	4159755	Labile essential hypertension
	4263067	Low-renin essential hypertension
	317898	Malignant essential hypertension
	45757787	Postpartum pre-existing essential hypertension
	4180283	Systolic essential hypertension
Diabetes	201826	Type 2 diabetes mellitus
	201254	Type 1 diabetes mellitus
	443731	Renal disorder due to type 2 diabetes mellitus
	200687	Renal disorder due to type 1 diabetes mellitus
	443729	Peripheral circulatory disorder due to type 2 diabetes mellitus
	318712	Peripheral circulatory disorder due to type 1 diabetes mellitus
	376065	Disorder of nervous system due to type 2 diabetes mellitus
	377821	Disorder of nervous system due to type 1 diabetes mellitus
	443733	Disorder of eye due to type 2 diabetes mellitus
	42538169	Disorder of eye due to type 1 diabetes mellitus
	443732	Disorder due to type 2 diabetes mellitus
	435216	Disorder due to type 1 diabetes mellitus
Osteoporosis	80502	Osteoporosis
	37204244	X-linked osteoporosis with fractures
	4109181	Osteoporosis with pseudoglioma

	44783850	Osteoporosis circumscripta
	36716194	Osteoporosis and oculocutaneous hypopigmentation syndrome
Chronic kidney disease	46271022	Chronic kidney disease
	75865	Disorder of the urinary system
	197331	Disorder of urinary tract
Skin Ulcer	4262920	Skin ulcer
	46269755	Chronic non-pressure ulcer of calf extending to fat level
	46269752	Chronic non-pressure ulcer of ankle extending to fat level
Ischeamic heart disease	4185932	Ischeamic heart disease
Heart Failure	316139	Heart failure
Cerebrovascular disease	381591	Cerebrovascular disease
Peripheral vascular disease	321052	Peripheral vascular disease
Atrial fibrilation	313217	Atrial fibrilation
Heart valve disease	4281749	Heart valve disorder
Hypotension/syncope	317002, 40350983	Low blood pressure
	40316030	Hypotension
	319041	Orthostatic hypotension
	135360, 40498271	Syncope
Foot problem	4101512	Foot problem
	4268887	Chiropody follow-up
	4053100	Domiciliary chiropody
	4136647	Seen by community-based podiatrist
	4138349	Seen by community-based podiatry service
	4140790	Seen by hospital-based podiatrist
	4140924	Seen by hospital-based podiatry service
	42539590	Seen by podiatric surgeon
	4083436	Seen by podiatrist
	4139895	Seen by podiatry service
	4085778	Seen in chiropody clinic
	4139217	Under care of community-based podiatrist
	4139218	Under care of hospital-based podiatrist
	42539494	Under care of podiatric surgeon
	4139705	Under care of podiatrist
	4067069	Callosity
Arthritis	4291025	Arthritis

	40555828	Arthritis
Chronic Respiratory disease	4063381	Chronic disease of the respiratory system
	261325	Pulmonary emphysema
	255573	Chronic obstructive lung disease
	317009	Asthma
Peptic ulcer	4027663	Peptic ulcer
	4057060	Acute Peptic ulcer
	4134146	Chronic Petic ulcer
Thyroid disease	141253	Disorder of thyroid gland
	4194160	Thyroid function tests abnormal
Fragility fracture	44791986	Fragility fracture
	40480160	Osteoporotic fracture
	4001142	Osteopathies, chondropathies and acquired musculoskeletal deformities
	44791986	Fragility fracture
	4174520	Fracture of vertebral column
	4050747	Fracture of upper limb
	4053828	Fracture of thoracic spine
	4302740	Fracture of sternum
	4142905	Fracture of rib
	4013613	Fracture of lumbar spine and/or pelvis
	4278672	Fracture of forearm
	442560	Fracture of femur
	4129393	Fracture of cervical spine
	4015350	Fracture at wrist and/or hand level
	4001458	Fatigue fracture of vertebra
	4344386	Disorder of continuity of bone
	4222001	Collapse of vertebra
Urinary System disease	4127562	Infective cystitis
	81902	Urinary tract infectious disease
	198199	Pyelonephritis
	195862	Urethritis
	4183440	Subacute cystitis
	36715430	Sepsis due to urinary tract infection
	4159655	Infection of bladder catheter
	201338	Urethral fistula
	4284706	Urethrotrigonitis
	196464	Rapidly progressive glomerulonephritis

	4054992	Rapidly progressive nephritic syndrome
	4127562	Infective Cystitis
	194081	Acute cystitis
	4189531	Acute nephritis
	4286024	Acute pyelonephritis
	4056023	Acute pyonephrosis
	19351000	Acute glomerulonephritis
	4284564	Acute infectious tubulointerstitial nephritis
	4126301	Idiopathic crescentic glomerulonephritis
Dizziness	4223938	Dizziness
	433316	Dizziness and giddiness
	43021417	Dizziness due to drug
	42539141	Dizziness following neck extension
	45769954	Dizziness on lying still
	44806935	Dizziness on neck extension
	4250121	Dizziness on standing up
	1333255	Dizziness or light-headedness
	4012520	Dizziness present
	4198449	Dizzy spells
	1340313	Exacerbation of dizziness
	4012691	Exertional dizziness
	905035	Fainting or dizziness
	4297376	Lightheadedness
	4337455	Multisensory dizziness
	4097171	Oscillation of surroundings
	4011333	Persistent postural perceptual dizziness
	4012243	Postural dizziness
	40768436	Things occurring with dizziness, loss of balance or spinning sensation [PhenX]
Parkinsonism and tremor	381270	Parkinson's disease
	36716783	Atypical Parkinsonism
	37110549	Functional parkinsonism
	4140090	Parkinsonism
	372604	Movement disorder
	443782	Tremor

Appendix II. Supplementary Tables

Appendix II. Table 1. Distribution of cancer types by database.

Cancer type	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
Solid tumors	n	%	n	%	n	%	n	%	n	%	n	%
Breast Cancer	5681	24%	14216	27%	24245	23%	495	15%	44196	28%	1054	36%
Colorectal Cancer	4825	20%	9656	18%	24981	24%	668	20%	20755	13%	307	10%
Endometrial	557	2%	1481	3%	3170	3%	128	4%	1874	1%	42	1%
Lung Cancer	5207	22%	7196	13%	12220	12%	201	6%	16528	11%	376	13%
Ovarian Cancer	429	2%	1417	3%	2843	3%	196	6%	4358	3%	32	1%
Pancreatic Cancer	1172	5%	1898	4%	5809	6%	179	5%	5603	4%	102	3%
Prostate	3725	15%	11798	22%	17272	17%	913	28%	40449	26%	740	25%
Blood tumors												
Leukaemia	917	4%	2092	4%	4304	4%	193	6%	6716	4%	140	5%
Lymphoma	1101	5%	2386	4%	7247	7%	215	7%	11040	7%	100	3%
Multiple Myeloma	456	2%	1172	2%	2522	2%	94	3%	3837	2%	60	2%

All values are N (%) unless otherwise stated. Percentage based on overall cancer counts by database. NA=Count <5.

Appendix II. Table 2. Patient characteristics and prevalence of frailty and polypharmacy by age groups.

Variable	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
Age group: 18 to 44						
Median Age	39	39	40	38	37	36
Sex: Female	895 (78.4%)	1817 (76.3%)	5154 (70.5%)	202 (76.5%)	6429 (75.3%)	159 (63.3%)
Sex: Male	247 (21.6%)	564 (23.7%)	2159 (29.5%)	62 (23.5%)	2106 (24.7%)	92 (36.7%)
Sex: None	NA	NA	NA	NA	5 (0.1%)	NA
Median frailty score	0.028	0.028	0.028	0.083	0.028	0.028
Frailty category: Fit	1103 (96.6%)	2255 (94.7%)	6720 (91.9%)	192 (72.7%)	7872 (92.2%)	236 (94%)
Frailty Category: Mild	37 (3.2%)	121 (5.1%)	552 (7.5%)	68 (25.8%)	610 (7.1%)	15 (6%)
Frailty category: Moderate	NA (NA%)	NA (NA%)	37 (0.5%)	NA (NA%)	58 (0.7%)	0 (0%)
Frailty category: Severe	0 (0%)	NA (NA%)	NA (NA%)	NA (NA%)	0 (0%)	0 (0%)
Median number of medications	1	2	2	2	1	2
Polypharmacy >=5	126 (11%)	481 (20.2%)	1269 (17.4%)	40 (15.2%)	390 (4.6%)	54 (21.5%)
Polypharmacy >=10	14 (1.2%)	113 (4.7%)	185 (2.5%)	NA (NA%)	33 (0.4%)	8 (3.2%)

Variable	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
Age group: 45 to 64						
Median Age	58	58	57	58	58	58
Sex: Female	4740 (59.6%)	10483 (61.9%)	20779 (56%)	732 (55.3%)	30292 (58.3%)	562 (62.2%)
Sex: Male	3209 (40.4%)	6462 (38.1%)	16345 (44%)	591 (44.7%)	21595 (41.6%)	342 (37.8%)
Sex: None	NA	NA	NA	NA	37 (0.1%)	NA
Median frailty score	0.028	0.056	0.056	0.111	0.028	0.056
Frailty category: Fit	7116 (89.5%)	14464 (85.4%)	28800 (77.6%)	765 (57.8%)	44080 (84.9%)	767 (84.8%)
Frailty Category: Mild	760 (9.6%)	2168 (12.8%)	7098 (19.1%)	456 (34.5%)	6380 (12.3%)	128 (14.2%)
Frailty category: Moderate	70 (0.9%)	286 (1.7%)	1092 (2.9%)	88 (6.7%)	1264 (2.4%)	9 (1%)
Frailty category: Severe	NA (NA%)	27 (0.2%)	134 (0.4%)	14 (1.1%)	200 (0.4%)	0 (0%)
Median number of medications	2	3	3	3	1	3
Polypharmacy >=5	2235 (28.1%)	6371 (37.6%)	13148 (35.4%)	351 (26.5%)	6166 (11.9%)	328 (36.3%)
Polypharmacy >=10	590 (7.4%)	2056 (12.1%)	3635 (9.8%)	30 (2.3%)	921 (1.8%)	67 (7.4%)

Variable	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
Age group: 65 to 74						
Median Age	70	70	70	69	69	70
Sex: Female	3729 (46.7%)	7705 (44.7%)	11104 (39.9%)	466 (45.7%)	19119 (44%)	395 (47.6%)
Sex: Male	4263 (53.3%)	9551 (55.3%)	16758 (60.1%)	554 (54.3%)	24336 (56%)	434 (52.4%)
Sex: None	NA	NA	NA	NA	17 (0%)	NA
Median frailty score	0.083	0.083	0.111	0.167	0.056	0.083
Frailty category: Fit	6187 (77.4%)	12321 (71.4%)	15075 (54.1%)	314 (30.8%)	33447 (76.9%)	614 (74.1%)
Frailty Category: Mild	1561 (19.5%)	4059 (23.5%)	9780 (35.1%)	436 (42.7%)	7454 (17.1%)	199 (24%)
Frailty category: Moderate	228 (2.9%)	753 (4.4%)	2500 (9%)	209 (20.5%)	2110 (4.9%)	15 (1.8%)
Frailty category: Severe	16 (0.2%)	123 (0.7%)	507 (1.8%)	61 (6%)	461 (1.1%)	NA (NA%)
Median number of medications	4	5	6	4	1	4
Polypharmacy >=5	3711 (46.4%)	9739 (56.4%)	17447 (62.6%)	481 (47.2%)	8420 (19.4%)	391 (47.2%)

Variable	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
Polypharmacy >=10	1171 (14.7%)	3749 (21.7%)	6578 (23.6%)	79 (7.7%)	1802 (4.1%)	103 (12.4%)
Age group: 75 to 84						
Median Age	79	79	79	78	79	79
Sex: Female	2499 (45.1%)	6001 (45.8%)	9812 (42.9%)	261 (45.5%)	18537 (43.2%)	296 (43.4%)
Sex: Male	3046 (54.9%)	7098 (54.2%)	13085 (57.1%)	312 (54.5%)	24372 (56.8%)	386 (56.6%)
Sex: None	NA	NA	NA	NA	28 (0.1%)	NA
Median frailty score	0.111	0.111	0.167	0.222	0.083	0.111
Frailty category: Fit	3220 (58.1%)	6943 (53%)	6732 (29.4%)	99 (17.3%)	29345 (68.3%)	423 (62%)
Frailty Category: Mild	1801 (32.5%)	4568 (34.9%)	9559 (41.7%)	218 (38%)	8906 (20.7%)	237 (34.8%)
Frailty category: Moderate	461 (8.3%)	1337 (10.2%)	4905 (21.4%)	189 (33%)	3515 (8.2%)	22 (3.2%)
Frailty category: Severe	63 (1.1%)	251 (1.9%)	1701 (7.4%)	67 (11.7%)	1171 (2.7%)	0 (0%)
Median number of medications	6	7	8	5	1	5
Polypharmacy >=5	3383 (61%)	9518 (72.7%)	18190 (79.4%)	317 (55.3%)	10734 (25%)	375 (55%)

Variable	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
Polypharmacy >=10	1316 (23.7%)	4200 (32.1%)	8752 (38.2%)	63 (11%)	2810 (6.5%)	108 (15.8%)
Age group: 85 to 120						
Median Age	88	88	88	87	87	88
Sex: Female	946 (53.8%)	2526 (53.3%)	6330 (53.7%)	74 (56.9%)	5618 (50%)	138 (46.3%)
Sex: Male	813 (46.2%)	2214 (46.7%)	5465 (46.3%)	56 (43.1%)	5605 (49.9%)	160 (53.7%)
Sex: None	NA	NA	NA	NA	13 (0.1%)	NA
Median frailty score	0.139	0.167	0.25	0.25	0.111	0.111
Frailty category: Fit	726 (41.3%)	1774 (37.4%)	1598 (13.5%)	10 (7.7%)	5872 (52.3%)	179 (60.1%)
Frailty Category: Mild	727 (41.3%)	1914 (40.4%)	4064 (34.5%)	44 (33.8%)	2916 (26%)	94 (31.5%)
Frailty category: Moderate	267 (15.2%)	831 (17.5%)	3876 (32.9%)	54 (41.5%)	1679 (14.9%)	21 (7%)
Frailty category: Severe	39 (2.2%)	221 (4.7%)	2257 (19.1%)	22 (16.9%)	769 (6.8%)	NA (NA%)
Median number of medications	6	8	9	5	3	4
Polypharmacy >=5	1190 (67.7%)	3796 (80.1%)	10093 (85.6%)	74 (56.9%)	4275 (38%)	140 (47%)
Polypharmacy >=10	461 (26.2%)	1836 (38.7%)	5304 (45%)	8 (6.2%)	1305 (11.6%)	41 (13.8%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 3 One-year hospitalisations rate by age group**.**

Database	Hospitalisation Rate	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
SIDIAP	18-44	1.38	1.92	2.16	NA	1.77	2.05
	45-64	1.25	1.62	2.03	2.22	1.57	1.79
	65-74	1.10	1.44	1.73	2.09	1.37	1.53
	75-84	0.95	1.29	1.56	1.68	1.32	1.44
	85+	0.79	1.02	1.18	1.27	1.11	1.16
EBB	18-44	4.03	3.94	NA	NA	5.92	NA
	45-64	3.49	4.05	3.13	4.25	3.92	4.38
	65-74	2.77	3.19	3.41	4.06	3.33	3.85
	75-84	2.67	2.40	3.20	3.43	2.86	3.92
	85+	1.33	2.66	3.24	3.21	3.36	2.43

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 4. One-year mortality risk by age group.

Database	Mortality Rate	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
IPCI	18-44	0.09	NA	NA	NA	0.14	NA
	45-64	0.18	0.27	0.35	NA	0.28	0.37
	65-74	0.26	0.34	0.43	NA	0.34	0.42
	75-84	0.39	0.45	0.51	0.56	0.46	0.53

Database	Mortality Rate	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
	85+	0.56	0.61	0.60	0.75	0.63	0.68
CPRD GOLD	18-44	0.12	0.29	NA	NA	0.23	0.37
	45-64	0.17	0.26	0.35	0.28	0.29	0.40
	65-74	0.25	0.36	0.41	0.50	0.36	0.46
	75-84	0.37	0.48	0.54	0.59	0.48	0.55
	85+	0.57	0.59	0.64	0.63	0.61	0.66
SIDIAP	18-44	0.09	0.11	0.28	NA	0.14	0.20
	45-64	0.18	0.24	0.37	0.52	0.27	0.34
	65-74	0.24	0.31	0.42	0.57	0.33	0.39
	75-84	0.34	0.42	0.54	0.67	0.46	0.52
	85+	0.57	0.66	0.74	0.8	0.71	0.75
EBB	18-44	0.04	0.10	NA	NA	NA	NA
	45-64	0.13	0.12	0.11	NA	0.16	NA
	65-74	0.17	0.21	0.19	0.25	0.22	0.25
	75-84	0.25	0.23	0.32	0.35	0.30	0.36
	85+		0.743	0.619	0.789	0.726	

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count <5.

Appendix II. Table 5 Characteristics of women and men with incident selected cancers and prevalence of frailty and polypharmacy by sex.

Variable	IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium

	Women N= 12,810	Men N= 11,579	Women N= 28,532	Men N= 25,889	Women N= 53,191	Men N= 53,819	Women N= 1735	Men N= 1575	Women N= 79,995	Men N= 78,014	Women N= 1550	Men N= 1414
Median Age	67	70	67	71	65	70	63	67	66	71	66	71
Age Group: 18 to 44	895 (7%)	247 (2.1%)	1817 (6.4%)	564 (2.2%)	5154 (9.7%)	2159 (4%)	202 (11.6%)	62 (3.9%)	6429 (8%)	2106 (2.7%)	159 (10.3%)	92 (6.5%)
Age Group: 45 to 64	4740 (37%)	3209 (27.7%)	10483 (36.7%)	6462 (25%)	20779 (39.1%)	16345 (30.4%)	732 (42.2%)	591 (37.5%)	30292 (37.9%)	21595 (27.7%)	562 (36.3%)	342 (24.2%)
Age Group: 65 to 74	3729 (29.1%)	4263 (36.8%)	7705 (27%)	9551 (36.9%)	11104 (20.9%)	16758 (31.1%)	466 (26.9%)	554 (35.2%)	19119 (23.9%)	24336 (31.2%)	395 (25.5%)	434 (30.7%)
Age Group: 75 to 84	2499 (19.5%)	3046 (26.3%)	6001 (21%)	7098 (27.4%)	9812 (18.4%)	13085 (24.3%)	261 (15%)	312 (19.8%)	18537 (23.2%)	24372 (31.2%)	296 (19.1%)	386 (27.3%)
Age Group: 85 to 120	946 (7.4%)	813 (7%)	2526 (8.9%)	2214 (8.6%)	6330 (11.9%)	5465 (10.2%)	74 (4.3%)	56 (3.6%)	5618 (7%)	5605 (7.2%)	138 (8.9%)	160 (11.3%)
Median frailty score	0.056	0.056	0.083	0.083	0.111	0.111	0.167	0.139	0.056	0.056	0.083	0.083
Frailty category: Fit	9465 (73.9%)	8889 (76.8%)	19699 (69%)	18058 (69.8%)	29437 (55.3%)	29506 (54.8%)	675 (38.9%)	705 (44.8%)	61360 (76.7%)	59182 (75.9%)	1155 (74.5%)	1064 (75.2%)
Frailty Category: Mild	2639 (20.6%)	2247 (19.4%)	6561 (23%)	6269 (24.2%)	14588 (27.4%)	16466 (30.6%)	633 (36.5%)	589 (37.4%)	12532 (15.7%)	13718 (17.6%)	347 (22.4%)	326 (23.1%)
Frailty category: Moderate	626 (4.9%)	402 (3.5%)	1866 (6.5%)	1345 (5.2%)	6441 (12.1%)	5969 (11.1%)	309 (17.8%)	234 (14.9%)	4567 (5.7%)	4051 (5.2%)	44 (2.8%)	23 (1.6%)

Frailty category: Severe	80 (0.6%)	41 (0.4%)	406 (1.4%)	217 (0.8%)	2725 (5.1%)	1878 (3.5%)	118 (6.8%)	47 (3%)	1536 (1.9%)	1063 (1.4%)	NA (NA%)	NA (NA%)
Median number of medications	3	4	5	5	5	6	3	4	1	1	4	4
Polypharmacy >=5	5207 (40.6%)	5438 (47%)	14922 (52.3%)	14983 (57.9%)	27715 (52.1%)	32435 (60.3%)	597 (34.4%)	666 (42.3%)	14122 (17.7%)	15832 (20.3%)	657 (42.4%)	631 (44.6%)
Polypharmacy >=10	1661 (13%)	1891 (16.3%)	6113 (21.4%)	5841 (22.6%)	11024 (20.7%)	13430 (25%)	89 (5.1%)	94 (6%)	3269 (4.1%)	3588 (4.6%)	167 (10.8%)	160 (11.3%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 6 Prevalence of conditions included in the frailty score by sex.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
Sex	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Disease State												
Arthritis	1051 (8.2%)	726 (6.3%)	3201 (11.2%)	3006 (11.6%)	6591 (12.4%)	5758 (10.7%)	676 (39%)	553 (35.1%)	8198 (10.2%)	7146 (9.2%)	279 (18%)	236 (16.7%)
Atrial fibrillation	646 (5%)	863 (7.5%)	1446 (5.1%)	2402 (9.3%)	3823 (7.2%)	5864 (10.9%)	0 (0%)	0 (0%)	2507 (3.1%)	3618 (4.6%)	0 (0%)	0 (0%)
Chronic kidney disease	4608 (36%)	2741 (23.7%)	9495 (33.3%)	7248 (28%)	25327 (47.6%)	23645 (43.9%)	1138 (65.6%)	740 (47%)	22435 (28%)	28547 (36.6%)	424 (27.4%)	273 (19.3%)
Cerebrovascular disease	753 (5.9%)	834 (7.2%)	1305 (4.6%)	1753 (6.8%)	1946 (3.7%)	3460 (6.4%)	248 (14.3%)	205 (13%)	4980 (6.2%)	7058 (9%)	71 (4.6%)	117 (8.3%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
Sex	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Diabetes	1373 (10.7%)	1637 (14.1%)	2982 (10.5%)	3764 (14.5%)	8270 (15.5%)	13587 (25.2%)	254 (14.6%)	299 (19%)	9401 (11.8%)	13088 (16.8%)	202 (13%)	259 (18.3%)
Foot problems	0 (0%)	0 (0%)	1805 (6.3%)	1770 (6.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	942 (7.4%)	569 (4.9%)	3733 (13.1%)	2182 (8.4%)	7919 (14.9%)	5521 (10.3%)	395 (22.8%)	336 (21.3%)	6285 (7.9%)	4376 (5.6%)	93 (6%)	41 (2.9%)
Heart failure	422 (3.3%)	472 (4.1%)	556 (1.9%)	910 (3.5%)	3746 (7%)	4768 (8.9%)	492 (28.4%)	551 (35%)	5296 (6.6%)	6556 (8.4%)	78 (5%)	95 (6.7%)
Heart valve disease	260 (2%)	297 (2.6%)	714 (2.5%)	861 (3.3%)	3411 (6.4%)	4252 (7.9%)	74 (4.3%)	85 (5.4%)	4150 (5.2%)	4631 (5.9%)	22 (1.4%)	28 (2%)
Hypertension	3543 (27.7%)	3296 (28.5%)	6935 (24.3%)	7727 (29.8%)	20309 (38.2%)	27102 (50.4%)	869 (50.1%)	903 (57.3%)	29465 (36.8%)	34456 (44.2%)	729 (47%)	778 (55%)
Hypotension	856 (6.7%)	891 (7.7%)	1109 (3.9%)	1106 (4.3%)	1140 (2.1%)	1508 (2.8%)	39 (2.2%)	21 (1.3%)	2266 (2.8%)	1392 (1.8%)	35 (2.3%)	33 (2.3%)
Ischaemic heart disease	765 (6%)	1383 (11.9%)	1461 (5.1%)	2996 (11.6%)	2170 (4.1%)	6183 (11.5%)	426 (24.6%)	577 (36.6%)	7164 (9%)	13205 (16.9%)	82 (5.3%)	165 (11.7%)
Osteoporosis	632 (4.9%)	175 (1.5%)	1942 (6.8%)	386 (1.5%)	7345 (13.8%)	1310 (2.4%)	228 (13.1%)	31 (2%)	8205 (10.3%)	2355 (3%)	270 (17.4%)	83 (5.9%)
Parkinsonism & tremor	61 (0.5%)	83 (0.7%)	852 (3%)	857 (3.3%)	2083 (3.9%)	2305 (4.3%)	115 (6.6%)	70 (4.4%)	3144 (3.9%)	2755 (3.5%)	76 (4.9%)	56 (4%)
Peptic ulcer	86 (0.7%)	113 (1%)	333 (1.2%)	524 (2%)	831 (1.6%)	1724 (3.2%)	294 (16.9%)	330 (21%)	1574 (2%)	1992 (2.6%)	39 (2.5%)	36 (2.5%)
Peripheral vascular disease	351 (2.7%)	510 (4.4%)	427 (1.5%)	715 (2.8%)	1063 (2%)	4035 (7.5%)	82 (4.7%)	163 (10.3%)	3346 (4.2%)	6082 (7.8%)	13 (0.8%)	42 (3%)
Respiratory disease	1889 (14.7%)	1734 (15%)	6186 (21.7%)	5424 (21%)	7524 (14.1%)	12552 (23.3%)	783 (45.1%)	660 (41.9%)	17522 (21.9%)	16803 (21.5%)	477 (30.8%)	520 (36.8%)
Skin ulcer	367 (2.9%)	256 (2.2%)	272 (1%)	263 (1%)	1479 (2.8%)	1541 (2.9%)	50 (2.9%)	39 (2.5%)	1308 (1.6%)	1252 (1.6%)	10 (0.6%)	NA (NA%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
Sex	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Thyroid disease	907 (7.1%)	276 (2.4%)	2978 (10.4%)	954 (3.7%)	10247 (19.3%)	3373 (6.3%)	623 (35.9%)	117 (7.4%)	19403 (24.3%)	9820 (12.6%)	289 (18.6%)	88 (6.2%)
Urinary system disease	3029 (23.6%)	1175 (10.1%)	4499 (15.8%)	2037 (7.9%)	18919 (35.6%)	9984 (18.6%)	562 (32.4%)	275 (17.5%)	12051 (15.1%)	9261 (11.9%)	155 (10%)	82 (5.8%)
Symptoms/Signs												
Dyspnoea	1417 (11.1%)	1232 (10.6%)	6049 (21.2%)	5784 (22.3%)	4730 (8.9%)	4257 (7.9%)	19 (1.1%)	16 (1%)	4223 (5.3%)	3956 (5.1%)	6 (0.4%)	5 (0.4%)
Dizziness	1354 (10.6%)	954 (8.2%)	4200 (14.7%)	3087 (11.9%)	10335 (19.4%)	7563 (14.1%)	275 (15.9%)	134 (8.5%)	7867 (9.8%)	5900 (7.6%)	102 (6.6%)	61 (4.3%)
Falls	0 (0%)	0 (0%)	2980 (10.4%)	1688 (6.5%)	3386 (6.4%)	1995 (3.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (0.5%)	7 (0.5%)
Memory & Cognitive problems	592 (4.6%)	589 (5.1%)	1214 (4.3%)	1132 (4.4%)	4663 (8.8%)	4373 (8.1%)	54 (3.1%)	49 (3.1%)	2871 (3.6%)	2611 (3.3%)	36 (2.3%)	37 (2.6%)
Sleep disturbance	1659 (13%)	1169 (10.1%)	3409 (11.9%)	2584 (10%)	9535 (17.9%)	9725 (18.1%)	607 (35%)	515 (32.7%)	8421 (10.5%)	8233 (10.6%)	539 (34.8%)	387 (27.4%)
Urinary incontinence	1703 (13.3%)	1382 (11.9%)	3560 (12.5%)	2412 (9.3%)	8844 (16.6%)	4761 (8.8%)	208 (12%)	19 (1.2%)	6282 (7.9%)	4386 (5.6%)	79 (5.1%)	73 (5.2%)
Weight loss & anorexia	912 (7.1%)	937 (8.1%)	1414 (5%)	1362 (5.3%)	2472 (4.6%)	3395 (6.3%)	24 (1.4%)	8 (0.5%)	2564 (3.2%)	2462 (3.2%)	9 (0.6%)	10 (0.7%)
Disability												
Activity limitation	0 (0%)	0 (0%)	34 (0.1%)	26 (0.1%)	1916 (3.6%)	1843 (3.4%)	NA (NA%)	0 (0%)	NA (NA%)	NA (NA%)	0 (0%)	0 (0%)
Hearing impairment	649 (5.1%)	838 (7.2%)	2308 (8.1%)	3165 (12.2%)	5890 (11.1%)	7262 (13.5%)	298 (17.2%)	359 (22.8%)	4101 (5.1%)	4674 (6%)	7 (0.5%)	9 (0.6%)
Housebound	0 (0%)	0 (0%)	519 (1.8%)	263 (1%)	2569 (4.8%)	1805 (3.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
Sex	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Mobility transfer	0 (0%)	0 (0%)	580 (2%)	407 (1.6%)	528 (1%)	438 (0.8%)	NA (NA%)	0 (0%)	626 (0.8%)	539 (0.7%)	0 (0%)	0 (0%)
Requiring care	0 (0%)	0 (0%)	571 (2%)	339 (1.3%)	2508 (4.7%)	1770 (3.3%)	0 (0%)	0 (0%)	496 (0.6%)	450 (0.6%)	0 (0%)	0 (0%)
Social vulnerability	818 (6.4%)	676 (5.8%)	399 (1.4%)	281 (1.1%)	6021 (11.3%)	2760 (5.1%)	10 (0.6%)	NA (NA%)	165 (0.2%)	85 (0.1%)	14 (0.9%)	10 (0.7%)
Visual impairment	1929 (15.1%)	1897 (16.4%)	3165 (11.1%)	3125 (12.1%)	16848 (31.7%)	18094 (33.6%)	659 (38%)	547 (34.7%)	6077 (7.6%)	6469 (8.3%)	79 (5.1%)	85 (6%)
Abnormal laboratory value												
Anaemia	1205 (9.4%)	1059 (9.1%)	3011 (10.6%)	2189 (8.5%)	13732 (25.8%)	11952 (22.2%)	525 (30.3%)	220 (14%)	8322 (10.4%)	6876 (8.8%)	101 (6.5%)	118 (8.3%)

All values are N (%) unless otherwise stated. NA=Count s<5.

Appendix II. Table 7 Characteristics of fit individuals by sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N=9465	Men N=8889	Women N= 19,699	Men N= 18,058	Women N= 29,437	Men N= 29,506	Women N= 675	Men N= 705	Women N= 61,360	Men N=59,182	Women N= 1155	Men N=1064
Median Age	63	68	63	69	57	64	55	62	64	70	63	69
Age Group: 18 to 44	857 (9.1%)	246 (2.8%)	1713 (8.7%)	542 (3%)	4679 (15.9%)	2041 (6.9%)	143 (21.2%)	49 (7%)	5918 (9.6%)	1950 (3.3%)	149 (12.9%)	87 (8.2%)
Age Group: 45 to 64	4161 (44%)	2955 (33.2%)	8842 (44.9%)	5622 (31.1%)	16057 (54.5%)	12743 (43.2%)	398 (59%)	367 (52.1%)	26113 (42.6%)	17933 (30.3%)	476 (41.2%)	291 (27.3%)
Age Group: 65 to 74	2739 (28.9%)	3448 (38.8%)	5275 (26.8%)	7046 (39%)	5617 (19.1%)	9458 (32.1%)	106 (15.7%)	208 (29.5%)	14735 (24%)	18698 (31.6%)	290 (25.1%)	324 (30.5%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N=9465	Men N=8889	Women N= 19,699	Men N= 18,058	Women N= 29,437	Men N= 29,506	Women N= 675	Men N= 705	Women N= 61,360	Men N=59,182	Women N= 1155	Men N=1064
Age Group: 75 to 84	1337 (14.1%)	1883 (21.2%)	2971 (15.1%)	3972 (22%)	2365 (8%)	4367 (14.8%)	25 (3.7%)	74 (10.5%)	12065 (19.7%)	17260 (29.2%)	168 (14.5%)	255 (24%)
Age Group: 85 to 120	370 (3.9%)	356 (4%)	898 (4.6%)	876 (4.9%)	708 (2.4%)	890 (3%)	NA (NA%)	7 (1%)	2529 (4.1%)	3341 (5.6%)	72 (6.2%)	107 (10.1%)
Median frailty score	0.056	0.056	0.056	0.056	0.056	0.056	0.083	0.083	0.028	0.028	0.056	0.056
Median number of medications	2	3	3	4	2	3	1	2	0	1	3	3

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 8 Characteristics of Individuals with mild frailty by sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N= 2639	Men N= 2247	Women N= 6561	Men N= 6269	Women N= 14,588	Men N= 16,466	Women N= 633	Men N= 589	Women N= 12,532	Men N= 13,718	Women N= 347	Men N= 326
Median Age	74	76	74	75	72	74	64	68	72	73	74	75
Age Group: 18 to 44	36 (1.4%)	NA (NA%)	100 (1.5%)	21 (0.3%)	447 (3.1%)	105 (0.6%)	55 (8.7%)	13 (2.2%)	461 (3.7%)	148 (1.1%)	10 (2.9%)	5 (1.5%)
Age Group: 45 to 64	525 (19.9%)	235 (10.5%)	1405 (21.4%)	763 (12.2%)	4056 (27.8%)	3042 (18.5%)	267 (42.2%)	189 (32.1%)	3386 (27%)	2991 (21.8%)	82 (23.6%)	46 (14.1%)
Age Group: 65 to 74	840 (31.8%)	721 (32.1%)	1946 (29.7%)	2113 (33.7%)	4081 (28%)	5699 (34.6%)	194 (30.6%)	242 (41.1%)	3162 (25.2%)	4289 (31.3%)	93 (26.8%)	106 (32.5%)
Age Group: 75 to 84	859 (32.6%)	942 (41.9%)	2118 (32.3%)	2450 (39.1%)	3990 (27.4%)	5569 (33.8%)	94 (14.8%)	124 (21.1%)	3979 (31.8%)	4924 (35.9%)	115 (33.1%)	122 (37.4%)
Age Group: 85 to 120	379 (14.4%)	348 (15.5%)	992 (15.1%)	922 (14.7%)	2013 (13.8%)	2051 (12.5%)	23 (3.6%)	21 (3.6%)	1544 (12.3%)	1366 (10%)	47 (13.5%)	47 (14.4%)

Median frailty score	0.167	0.167	0.167	0.167	0.167	0.167	0.167	0.167	0.167	0.167	0.167	0.167
Median number of medications	7	8	8	9	7	8	4	5	4	5	7	7

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 9 Characteristics of individuals with moderate frailty by sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N=626	Men N= 402	Women N= 1866	Men N= 1345	Women N= 6441	Men N= 5969	Women N= 309	Men N= 234	Women N= 4567	Men N= 4567	Women N= 44	Men N= 23
Median Age	79	79	79	79	81	80	73	74	78	77	79.5	75
Age Group: 18 to 44	NA (NA%)	0 (0%)	NA (NA%)	0 (0%)	25 (0.4%)	12 (0.2%)	NA (NA%)	0 (0%)	50 (1.1%)	8 (0.2%)	0 (0%)	0 (0%)
Age Group: 45 to 64	52 (8.3%)	18 (4.5%)	215 (11.5%)	71 (5.3%)	597 (9.3%)	495 (8.3%)	56 (18.1%)	32 (13.7%)	681 (14.9%)	583 (14.4%)	NA (NA%)	5 (21.7%)
Age Group: 65 to 74	139 (22.2%)	89 (22.1%)	412 (22.1%)	341 (25.4%)	1170 (18.2%)	1330 (22.3%)	123 (39.8%)	86 (36.8%)	1004 (22%)	1106 (27.3%)	11 (25%)	NA (NA%)
Age Group: 75 to 84	262 (41.9%)	199 (49.5%)	756 (40.5%)	581 (43.2%)	2469 (38.3%)	2436 (40.8%)	97 (31.4%)	92 (39.3%)	1800 (39.4%)	1710 (42.2%)	13 (29.5%)	9 (39.1%)
Age Group: 85 to 120	171 (27.3%)	96 (23.9%)	479 (25.7%)	352 (26.2%)	2180 (33.8%)	1696 (28.4%)	30 (9.7%)	24 (10.3%)	1032 (22.6%)	644 (15.9%)	16 (36.4%)	5 (21.7%)
Median frailty score	0.278	0.278	0.278	0.278	0.278	0.278	0.278	0.278	0.278	0.278	0.25	0.25
Median number of medications	9	10	11	11	10	11	5	7	7	7	11	10

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 10 Characteristics of individuals with severe frailty by sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N=80	Men N=41	Women N=406	Men N=217	Women N= 2725	Men N= 1878	Women N= 118	Men N= 47	Women N= 1536	Men N= 1063	Women N=NA	Men N=NA
Median Age	81	82	82.5	80	85	83	75.5	75	82	79	NA	NA
Age Group: 18 to 44	0 (0%)	0 (0%)	0 (0%)	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	0 (0%)	0 (0%)	0 (0%)	NA (NA%)	NA (NA%)
Age Group: 45 to 64	NA (NA%)	NA (NA%)	21 (5.2%)	6 (2.8%)	69 (2.5%)	65 (3.5%)	11 (9.3%)	NA (NA%)	112 (7.3%)	88 (8.3%)	NA (NA%)	NA (NA%)
Age Group: 65 to 74	11 (13.8%)	5 (12.2%)	72 (17.7%)	51 (23.5%)	236 (8.7%)	271 (14.4%)	43 (36.4%)	18 (38.3%)	218 (14.2%)	243 (22.9%)	NA (NA%)	NA (NA%)
Age Group: 75 to 84	41 (51.2%)	22 (53.7%)	156 (38.4%)	95 (43.8%)	988 (36.3%)	713 (38%)	45 (38.1%)	22 (46.8%)	693 (45.1%)	478 (45%)	NA (NA%)	NA (NA%)
Age Group: 85 to 120	26 (32.5%)	13 (31.7%)	157 (38.7%)	64 (29.5%)	1429 (52.4%)	828 (44.1%)	18 (15.3%)	NA (NA%)	513 (33.4%)	254 (23.9%)	NA (NA%)	NA (NA%)
Sex: Female	80 (100%)	0 (0%)	406 (100%)	0 (0%)	2725 (100%)	0 (0%)	118 (100%)	0 (0%)	1536 (100%)	0 (0%)	NA (NA%)	NA (NA%)
Sex: Male	0 (0%)	41 (100%)	0 (0%)	217 (100%)	0 (0%)	1878 (100%)	0 (0%)	47 (100%)	0 (0%)	1063 (100%)	NA (NA%)	NA (NA%)
Sex: None	NA	NA	NA	NA	NA	NA	NA	NA	0 (0%)	0 (0%)	NA	NA
Median frailty score	0.389	0.361	0.389	0.389	0.389	0.389	0.389	0.389	0.389	0.389	NA	NA
Median number of medications	11	12	14	14	13	14	8	8	9	8	NA	NA

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 11. Conditions of fit Individuals by sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N=9465	Men N=8889	Women N= 19,699	Men N= 18,058	Women N= 29,437	Men N= 29,506	Women N= 675	Men N= 705	Women N= 61,360	Men N=59,182	Women N= 1155	Men N=1064
Disease State												
Arthritis	511 (5.4%)	416 (4.7%)	1305 (6.6%)	1375 (7.6%)	2315 (7.9%)	2016 (6.8%)	144 (21.3%)	169 (24%)	3597 (5.9%)	3035 (5.1%)	155 (13.4%)	124 (11.7%)
Atrial fibrillation	170 (1.8%)	298 (3.4%)	294 (1.5%)	684 (3.8%)	234 (0.8%)	742 (2.5%)	0 (0%)	0 (0%)	635 (1%)	1052 (1.8%)	0 (0%)	0 (0%)
Chronic kidney disease	2210 (23.3%)	1281 (14.4%)	3597 (18.3%)	2962 (16.4%)	7493 (25.5%)	6850 (23.2%)	294 (43.6%)	179 (25.4%)	9683 (15.8%)	16794 (28.4%)	202 (17.5%)	137 (12.9%)
Cerebrovascular disease	208 (2.2%)	336 (3.8%)	292 (1.5%)	536 (3%)	174 (0.6%)	391 (1.3%)	18 (2.7%)	24 (3.4%)	1373 (2.2%)	2169 (3.7%)	29 (2.5%)	49 (4.6%)
Diabetes	490 (5.2%)	700 (7.9%)	964 (4.9%)	1413 (7.8%)	1380 (4.7%)	3303 (11.2%)	18 (2.7%)	40 (5.7%)	3055 (5%)	4948 (8.4%)	81 (7%)	120 (11.3%)
Foot problems	0 (0%)	0 (0%)	408 (2.1%)	444 (2.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	387 (4.1%)	299 (3.4%)	1508 (7.7%)	1005 (5.6%)	1535 (5.2%)	1754 (5.9%)	66 (9.8%)	106 (15%)	2148 (3.5%)	1553 (2.6%)	38 (3.3%)	16 (1.5%)
Heart failure	82 (0.9%)	108 (1.2%)	51 (0.3%)	122 (0.7%)	108 (0.4%)	272 (0.9%)	28 (4.1%)	54 (7.7%)	1027 (1.7%)	1510 (2.6%)	18 (1.6%)	21 (2%)
Heart valve disease	66 (0.7%)	100 (1.1%)	137 (0.7%)	207 (1.1%)	288 (1%)	520 (1.8%)	8 (1.2%)	10 (1.4%)	1459 (2.4%)	1583 (2.7%)	9 (0.8%)	12 (1.1%)
Hypertension	1691 (17.9%)	1842 (20.7%)	2993 (15.2%)	3942 (21.8%)	5095 (17.3%)	9062 (30.7%)	150 (22.2%)	238 (33.8%)	14670 (23.9%)	18530 (31.3%)	403 (34.9%)	470 (44.2%)
Hypotension	331 (3.5%)	393 (4.4%)	275 (1.4%)	270 (1.5%)	236 (0.8%)	180 (0.6%)	9 (1.3%)	NA (NA%)	736 (1.2%)	329 (0.6%)	15 (1.3%)	9 (0.8%)
Ischaemic heart disease	215 (2.3%)	594 (6.7%)	324 (1.6%)	969 (5.4%)	142 (0.5%)	898 (3%)	27 (4%)	87 (12.3%)	1811 (3%)	4704 (7.9%)	24 (2.1%)	63 (5.9%)
Osteoporosis	200 (2.1%)	62 (0.7%)	571 (2.9%)	92 (0.5%)	1405 (4.8%)	191 (0.6%)	9 (1.3%)	NA (NA%)	3704 (6%)	773 (1.3%)	133 (11.5%)	46 (4.3%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N=9465	Men N=8889	Women N= 19,699	Men N= 18,058	Women N= 29,437	Men N= 29,506	Women N= 675	Men N= 705	Women N= 61,360	Men N=59,182	Women N= 1155	Men N=1064
Parkinsonism & tremor	18 (0.2%)	32 (0.4%)	222 (1.1%)	266 (1.5%)	238 (0.8%)	366 (1.2%)	20 (3%)	11 (1.6%)	1085 (1.8%)	944 (1.6%)	27 (2.3%)	26 (2.4%)
Peptic ulcer	29 (0.3%)	52 (0.6%)	86 (0.4%)	180 (1%)	186 (0.6%)	451 (1.5%)	36 (5.3%)	79 (11.2%)	354 (0.6%)	590 (1%)	21 (1.8%)	18 (1.7%)
Peripheral vascular disease	81 (0.9%)	148 (1.7%)	87 (0.4%)	186 (1%)	88 (0.3%)	465 (1.6%)	NA (NA%)	14 (2%)	676 (1.1%)	1456 (2.5%)	NA (NA%)	15 (1.4%)
Respiratory disease	814 (8.6%)	835 (9.4%)	2430 (12.3%)	2180 (12.1%)	1966 (6.7%)	3343 (11.3%)	190 (28.1%)	206 (29.2%)	8486 (13.8%)	7665 (13%)	273 (23.6%)	294 (27.6%)
Skin ulcer	100 (1.1%)	77 (0.9%)	61 (0.3%)	64 (0.4%)	117 (0.4%)	167 (0.6%)	10 (1.5%)	10 (1.4%)	223 (0.4%)	216 (0.4%)	5 (0.4%)	0 (0%)
Thyroid disease	425 (4.5%)	123 (1.4%)	1265 (6.4%)	338 (1.9%)	3439 (11.7%)	888 (3%)	115 (17%)	17 (2.4%)	8830 (14.4%)	3548 (6%)	165 (14.3%)	41 (3.9%)
Symptoms/Signs												
Dyspnoea	551 (5.8%)	531 (6%)	1782 (9%)	1881 (10.4%)	665 (2.3%)	768 (2.6%)	NA (NA%)	NA (NA%)	1080 (1.8%)	973 (1.6%)	NA (NA%)	NA (NA%)
Dizziness	525 (5.5%)	390 (4.4%)	1423 (7.2%)	1033 (5.7%)	2768 (9.4%)	1993 (6.8%)	47 (7%)	17 (2.4%)	2382 (3.9%)	1705 (2.9%)	28 (2.4%)	26 (2.4%)
Falls	0 (0%)	0 (0%)	737 (3.7%)	423 (2.3%)	401 (1.4%)	226 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA (NA%)	NA (NA%)
Memory & Cognitive problems	180 (1.9%)	192 (2.2%)	304 (1.5%)	310 (1.7%)	360 (1.2%)	530 (1.8%)	NA (NA%)	6 (0.9%)	597 (1%)	633 (1.1%)	9 (0.8%)	19 (1.8%)
Sleep disturbance	670 (7.1%)	548 (6.2%)	1185 (6%)	902 (5%)	2322 (7.9%)	2604 (8.8%)	71 (10.5%)	105 (14.9%)	2857 (4.7%)	2726 (4.6%)	291 (25.2%)	213 (20%)
Urinary incontinence	675 (7.1%)	699 (7.9%)	1040 (5.3%)	863 (4.8%)	991 (3.4%)	519 (1.8%)	32 (4.7%)	NA (NA%)	2672 (4.4%)	2135 (3.6%)	27 (2.3%)	34 (3.2%)
Disability												
Activity limitation	0 (0%)	0 (0%)	NA (NA%)	NA (NA%)	248 (0.8%)	283 (1%)	0 (0%)	0 (0%)	0 (0%)	NA (NA%)	0 (0%)	0 (0%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N=9465	Men N=8889	Women N= 19,699	Men N= 18,058	Women N= 29,437	Men N= 29,506	Women N= 675	Men N= 705	Women N= 61,360	Men N=59,182	Women N= 1155	Men N=1064
Hearing impairment	238 (2.5%)	381 (4.3%)	783 (4%)	1261 (7%)	1259 (4.3%)	1950 (6.6%)	44 (6.5%)	75 (10.6%)	1957 (3.2%)	1967 (3.3%)	NA (NA%)	NA (NA%)
Housebound	0 (0%)	0 (0%)	103 (0.5%)	54 (0.3%)	63 (0.2%)	59 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	0 (0%)	68 (0.3%)	62 (0.3%)	32 (0.1%)	21 (0.1%)	0 (0%)	0 (0%)	139 (0.2%)	88 (0.1%)	0 (0%)	0 (0%)
Requiring care	0 (0%)	0 (0%)	153 (0.8%)	103 (0.6%)	97 (0.3%)	105 (0.4%)	0 (0%)	0 (0%)	42 (0.1%)	58 (0.1%)	0 (0%)	0 (0%)
Social vulnerability	203 (2.1%)	211 (2.4%)	102 (0.5%)	74 (0.4%)	1005 (3.4%)	462 (1.6%)	NA (NA%)	0 (0%)	58 (0.1%)	27 (0%)	13 (1.1%)	NA (NA%)
Visual impairment	792 (8.4%)	891 (10%)	925 (4.7%)	1099 (6.1%)	3692 (12.5%)	4826 (16.4%)	82 (12.1%)	109 (15.5%)	1336 (2.2%)	1603 (2.7%)	25 (2.2%)	33 (3.1%)
Abnormal laboratory value												
Anaemia	466 (4.9%)	420 (4.7%)	1053 (5.3%)	689 (3.8%)	4059 (13.8%)	2542 (8.6%)	163 (24.1%)	42 (6%)	2930 (4.8%)	1864 (3.1%)	44 (3.8%)	46 (4.3%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 12. Conditions of Individuals with Mild Frailty by Sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N= 2,639	Men N= 2,247	Women N= 6,561	Men N= 6,269	Women N= 14,588	Men N= 16,466	Women N= 633	Men N= 589	Women N= 12,532	Men N= 13,718	Women N= 347	Men N= 326
Disease State												
Arthritis	373 (14.1%)	237 (10.5%)	1246 (19%)	1196 (19.1%)	2470 (16.9%)	2356 (14.3%)	293 (46.3%)	245 (41.6%)	2437 (19.4%)	2453 (17.9%)	103 (29.7%)	101 (31%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N= 2,639	Men N= 2,247	Women N= 6,561	Men N= 6,269	Women N= 14,588	Men N= 16,466	Women N= 633	Men N= 589	Women N= 12,532	Men N= 13,718	Women N= 347	Men N= 326
Atrial fibrillation	297 (11.3%)	393 (17.5%)	651 (9.9%)	1173 (18.7%)	1032 (7.1%)	2218 (13.5%)	0 (0%)	0 (0%)	880 (7%)	1429 (10.4%)	0 (0%)	0 (0%)
Chronic kidney disease	1791 (67.9%)	1115 (49.6%)	3985 (60.7%)	3096 (49.4%)	9813 (67.3%)	10129 (61.5%)	455 (71.9%)	338 (57.4%)	7545 (60.2%)	7627 (55.6%)	182 (52.4%)	118 (36.2%)
Cerebrovascular disease	347 (13.1%)	363 (16.2%)	578 (8.8%)	798 (12.7%)	529 (3.6%)	1390 (8.4%)	68 (10.7%)	74 (12.6%)	1657 (13.2%)	2880 (21%)	32 (9.2%)	60 (18.4%)
Diabetes	598 (22.7%)	740 (32.9%)	1262 (19.2%)	1656 (26.4%)	3159 (21.7%)	6006 (36.5%)	90 (14.2%)	140 (23.8%)	3493 (27.9%)	5243 (38.2%)	98 (28.2%)	127 (39%)
Foot problems	0 (0%)	0 (0%)	735 (11.2%)	855 (13.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	361 (13.7%)	195 (8.7%)	1402 (21.4%)	812 (13%)	2702 (18.5%)	1936 (11.8%)	159 (25.1%)	141 (23.9%)	1935 (15.4%)	1604 (11.7%)	39 (11.2%)	21 (6.4%)
Heart failure	168 (6.4%)	221 (9.8%)	239 (3.6%)	457 (7.3%)	736 (5%)	1406 (8.5%)	169 (26.7%)	253 (43%)	1808 (14.4%)	2713 (19.8%)	40 (11.5%)	65 (19.9%)
Heart valve disease	116 (4.4%)	135 (6%)	320 (4.9%)	396 (6.3%)	950 (6.5%)	1522 (9.2%)	21 (3.3%)	31 (5.3%)	1368 (10.9%)	1812 (13.2%)	10 (2.9%)	10 (3.1%)
Hypertension	1362 (51.6%)	1175 (52.3%)	2688 (41%)	2938 (46.9%)	7860 (53.9%)	11438 (69.5%)	351 (55.5%)	433 (73.5%)	9265 (73.9%)	11216 (81.8%)	280 (80.7%)	286 (87.7%)
Hypotension	336 (12.7%)	359 (16%)	410 (6.2%)	485 (7.7%)	304 (2.1%)	472 (2.9%)	18 (2.8%)	9 (1.5%)	775 (6.2%)	515 (3.8%)	15 (4.3%)	19 (5.8%)
Ischaemic heart disease	356 (13.5%)	578 (25.7%)	622 (9.5%)	1383 (22.1%)	604 (4.1%)	2572 (15.6%)	139 (22%)	268 (45.5%)	2490 (19.9%)	5310 (38.7%)	44 (12.7%)	86 (26.4%)
Osteoporosis	279 (10.6%)	76 (3.4%)	818 (12.5%)	185 (3%)	2705 (18.5%)	461 (2.8%)	78 (12.3%)	10 (1.7%)	2233 (17.8%)	844 (6.2%)	110 (31.7%)	32 (9.8%)
Parkinsonism & tremor	27 (1%)	35 (1.6%)	323 (4.9%)	368 (5.9%)	596 (4.1%)	901 (5.5%)	29 (4.6%)	34 (5.8%)	906 (7.2%)	911 (6.6%)	39 (11.2%)	27 (8.3%)
Peptic ulcer	43 (1.6%)	46 (2%)	148 (2.3%)	237 (3.8%)	284 (1.9%)	646 (3.9%)	102 (16.1%)	127 (21.6%)	540 (4.3%)	735 (5.4%)	14 (4%)	16 (4.9%)
Peripheral vascular disease	150 (5.7%)	251 (11.2%)	178 (2.7%)	345 (5.5%)	306 (2.1%)	1575 (9.6%)	19 (3%)	58 (9.8%)	1177 (9.4%)	2639 (19.2%)	5 (1.4%)	22 (6.7%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N= 2,639	Men N= 2,247	Women N= 6,561	Men N= 6,269	Women N= 14,588	Men N= 16,466	Women N= 633	Men N= 589	Women N= 12,532	Men N= 13,718	Women N= 347	Men N= 326
Respiratory disease	770 (29.2%)	694 (30.9%)	2523 (38.5%)	2386 (38.1%)	2779 (19%)	5266 (32%)	322 (50.9%)	265 (45%)	5401 (43.1%)	5831 (42.5%)	169 (48.7%)	209 (64.1%)
Skin ulcer	145 (5.5%)	124 (5.5%)	97 (1.5%)	105 (1.7%)	336 (2.3%)	465 (2.8%)	10 (1.6%)	11 (1.9%)	387 (3.1%)	443 (3.2%)	NA (NA%)	NA (NA%)
Thyroid disease	337 (12.8%)	104 (4.6%)	1109 (16.9%)	437 (7%)	3750 (25.7%)	1356 (8.2%)	259 (40.9%)	48 (8.1%)	6540 (52.2%)	3924 (28.6%)	102 (29.4%)	40 (12.3%)
Urinary system disease	1282 (48.6%)	540 (24%)	1970 (30%)	949 (15.1%)	7201 (49.4%)	4232 (25.7%)	224 (35.4%)	131 (22.2%)	4279 (34.1%)	2354 (17.2%)	83 (23.9%)	47 (14.4%)
Symptoms/Signs												
Dyspnoea	564 (21.4%)	499 (22.2%)	2688 (41%)	2779 (44.3%)	1531 (10.5%)	1569 (9.5%)	NA (NA%)	6 (1%)	1430 (11.4%)	1543 (11.2%)	NA (NA%)	NA (NA%)
Dizziness	551 (20.9%)	411 (18.3%)	1658 (25.3%)	1353 (21.6%)	3860 (26.5%)	3077 (18.7%)	100 (15.8%)	54 (9.2%)	2673 (21.3%)	2224 (16.2%)	61 (17.6%)	32 (9.8%)
Falls	0 (0%)	0 (0%)	1180 (18%)	763 (12.2%)	944 (6.5%)	648 (3.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6 (1.7%)	NA (NA%)
Memory & Cognitive problems	245 (9.3%)	268 (11.9%)	464 (7.1%)	532 (8.5%)	1368 (9.4%)	1626 (9.9%)	12 (1.9%)	14 (2.4%)	918 (7.3%)	948 (6.9%)	19 (5.5%)	14 (4.3%)
Sleep disturbance	661 (25%)	460 (20.5%)	1333 (20.3%)	1133 (18.1%)	3556 (24.4%)	4025 (24.4%)	257 (40.6%)	216 (36.7%)	2925 (23.3%)	3270 (23.8%)	212 (61.1%)	154 (47.2%)
Urinary incontinence	651 (24.7%)	517 (23%)	1509 (23%)	1043 (16.6%)	2857 (19.6%)	1561 (9.5%)	67 (10.6%)	6 (1%)	1529 (12.2%)	1121 (8.2%)	39 (11.2%)	33 (10.1%)
Weight loss & anorexia	394 (14.9%)	371 (16.5%)	554 (8.4%)	572 (9.1%)	877 (6%)	1301 (7.9%)	9 (1.4%)	NA (NA%)	891 (7.1%)	936 (6.8%)	6 (1.7%)	NA (NA%)
Disability												
Activity limitation	0 (0%)	0 (0%)	6 (0.1%)	12 (0.2%)	639 (4.4%)	693 (4.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hearing impairment	267 (10.1%)	342 (15.2%)	902 (13.7%)	1351 (21.6%)	2103 (14.4%)	3034 (18.4%)	93 (14.7%)	158 (26.8%)	937 (7.5%)	1425 (10.4%)	NA (NA%)	6 (1.8%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women N= 2,639	Men N= 2,247	Women N= 6,561	Men N= 6,269	Women N= 14,588	Men N= 16,466	Women N= 633	Men N= 589	Women N= 12,532	Men N= 13,718	Women N= 347	Men N= 326
Housebound	0 (0%)	0 (0%)	211 (3.2%)	118 (1.9%)	430 (2.9%)	328 (2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	0 (0%)	206 (3.1%)	176 (2.8%)	105 (0.7%)	106 (0.6%)	0 (0%)	0 (0%)	162 (1.3%)	158 (1.2%)	0 (0%)	0 (0%)
Requiring care	0 (0%)	0 (0%)	213 (3.2%)	140 (2.2%)	475 (3.3%)	437 (2.7%)	0 (0%)	0 (0%)	172 (1.4%)	166 (1.2%)	0 (0%)	0 (0%)
Social vulnerability	370 (14%)	318 (14.2%)	150 (2.3%)	120 (1.9%)	1999 (13.7%)	1034 (6.3%)	NA (NA%)	NA (NA%)	64 (0.5%)	33 (0.2%)	0 (0%)	6 (1.8%)
Visual impairment	774 (29.3%)	775 (34.5%)	1330 (20.3%)	1398 (22.3%)	6659 (45.6%)	7952 (48.3%)	252 (39.8%)	241 (40.9%)	2222 (17.7%)	2721 (19.8%)	44 (12.7%)	47 (14.4%)
Abnormal laboratory value												
Anaemia	476 (18%)	452 (20.1%)	1137 (17.3%)	972 (15.5%)	4444 (30.5%)	4669 (28.4%)	196 (31%)	89 (15.1%)	2755 (22%)	2755 (20.1%)	42 (12.1%)	64 (19.6%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 13. Conditions of Individuals with Moderate Frailty by Sex and database

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Disease State												
Arthritis	142 (22.7%)	60 (14.9%)	499 (26.7%)	348 (25.9%)	1211 (18.8%)	1015 (17%)	163 (52.8%)	105 (44.9%)	1445 (31.6%)	1189 (29.4%)	18 (40.9%)	11 (47.8%)
Atrial fibrillation	144 (23%)	149 (37.1%)	359 (19.2%)	448 (33.3%)	1391 (21.6%)	1932 (32.4%)	0 (0%)	0 (0%)	594 (13%)	801 (19.8%)	0 (0%)	0 (0%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Chronic kidney disease	536 (85.6%)	307 (76.4%)	1532 (82.1%)	999 (74.3%)	5473 (85%)	4916 (82.4%)	274 (88.7%)	180 (76.9%)	3761 (82.4%)	3134 (77.4%)	36 (81.8%)	17 (73.9%)
Cerebrovascular disease	156 (24.9%)	117 (29.1%)	311 (16.7%)	337 (25.1%)	646 (10%)	1076 (18%)	100 (32.4%)	77 (32.9%)	1223 (26.8%)	1439 (35.5%)	8 (18.2%)	7 (30.4%)
Diabetes	238 (38%)	173 (43%)	584 (31.3%)	572 (42.5%)	2365 (36.7%)	3114 (52.2%)	83 (26.9%)	96 (41%)	1929 (42.2%)	2189 (54%)	20 (45.5%)	11 (47.8%)
Foot problems	0 (0%)	0 (0%)	496 (26.6%)	365 (27.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	162 (25.9%)	61 (15.2%)	619 (33.2%)	291 (21.6%)	2263 (35.1%)	1178 (19.7%)	108 (35%)	60 (25.6%)	1441 (31.6%)	884 (21.8%)	13 (29.5%)	NA (NA%)
Heart failure	135 (21.6%)	125 (31.1%)	183 (9.8%)	267 (19.9%)	1431 (22.2%)	1918 (32.1%)	192 (62.1%)	202 (86.3%)	1524 (33.4%)	1628 (40.2%)	17 (38.6%)	8 (34.8%)
Heart valve disease	64 (10.2%)	50 (12.4%)	175 (9.4%)	208 (15.5%)	1141 (17.7%)	1433 (24%)	19 (6.1%)	32 (13.7%)	847 (18.5%)	870 (21.5%)	NA (NA%)	5 (21.7%)
Hypertension	427 (68.2%)	255 (63.4%)	984 (52.7%)	723 (53.8%)	4943 (76.7%)	4924 (82.5%)	257 (83.2%)	191 (81.6%)	4061 (88.9%)	3677 (90.8%)	42 (95.5%)	21 (91.3%)
Hypotension	159 (25.4%)	119 (29.6%)	290 (15.5%)	275 (20.4%)	295 (4.6%)	495 (8.3%)	10 (3.2%)	NA (NA%)	482 (10.6%)	338 (8.3%)	5 (11.4%)	5 (21.7%)
Ischaemic heart disease	159 (25.4%)	190 (47.3%)	360 (19.3%)	520 (38.7%)	721 (11.2%)	1848 (31%)	168 (54.4%)	180 (76.9%)	1859 (40.7%)	2374 (58.6%)	12 (27.3%)	15 (65.2%)
Osteoporosis	129 (20.6%)	30 (7.5%)	414 (22.2%)	80 (5.9%)	2023 (31.4%)	415 (7%)	95 (30.7%)	12 (5.1%)	1462 (32%)	516 (12.7%)	23 (52.3%)	5 (21.7%)
Parkinsonism & tremor	15 (2.4%)	12 (3%)	214 (11.5%)	177 (13.2%)	706 (11%)	676 (11.3%)	40 (12.9%)	17 (7.3%)	718 (15.7%)	617 (15.2%)	9 (20.5%)	NA (NA%)
Peptic ulcer	12 (1.9%)	14 (3.5%)	79 (4.2%)	82 (6.1%)	212 (3.3%)	428 (7.2%)	100 (32.4%)	96 (41%)	397 (8.7%)	456 (11.3%)	NA (NA%)	NA (NA%)
Peripheral vascular disease	94 (15%)	99 (24.6%)	109 (5.8%)	137 (10.2%)	334 (5.2%)	1341 (22.5%)	32 (10.4%)	68 (29.1%)	922 (20.2%)	1452 (35.8%)	NA (NA%)	5 (21.7%)
Respiratory disease	263 (42%)	187 (46.5%)	967 (51.8%)	719 (53.5%)	1717 (26.7%)	2790 (46.7%)	180 (58.3%)	151 (64.5%)	2580 (56.5%)	2495 (61.6%)	33 (75%)	16 (69.6%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Skin ulcer	96 (15.3%)	45 (11.2%)	82 (4.4%)	63 (4.7%)	504 (7.8%)	490 (8.2%)	20 (6.5%)	13 (5.6%)	389 (8.5%)	385 (9.5%)	NA (NA%)	0 (0%)
Thyroid disease	119 (19%)	39 (9.7%)	453 (24.3%)	148 (11%)	2018 (31.3%)	779 (13.1%)	160 (51.8%)	38 (16.2%)	2910 (63.7%)	1714 (42.3%)	22 (50%)	6 (26.1%)
Urinary system disease	408 (65.2%)	180 (44.8%)	970 (52%)	416 (30.9%)	4149 (64.4%)	2541 (42.6%)	150 (48.5%)	80 (34.2%)	2424 (53.1%)	1248 (30.8%)	25 (56.8%)	7 (30.4%)
Symptoms/Signs												
Dyspnoea	247 (39.5%)	175 (43.5%)	1243 (66.6%)	941 (70%)	1453 (22.6%)	1233 (20.7%)	8 (2.6%)	8 (3.4%)	1077 (23.6%)	975 (24.1%)	0 (0%)	0 (0%)
Dizziness	243 (38.8%)	130 (32.3%)	858 (46%)	560 (41.6%)	2389 (37.1%)	1717 (28.8%)	82 (26.5%)	42 (17.9%)	1810 (39.6%)	1375 (33.9%)	12 (27.3%)	NA (NA%)
Falls	0 (0%)	0 (0%)	793 (42.5%)	392 (29.1%)	1097 (17%)	638 (10.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA (NA%)
Memory & Cognitive problems	134 (21.4%)	111 (27.6%)	308 (16.5%)	227 (16.9%)	1634 (25.4%)	1416 (23.7%)	22 (7.1%)	19 (8.1%)	845 (18.5%)	677 (16.7%)	8 (18.2%)	NA (NA%)
Sleep disturbance	286 (45.7%)	139 (34.6%)	674 (36.1%)	441 (32.8%)	2340 (36.3%)	2156 (36.1%)	180 (58.3%)	152 (65%)	1768 (38.7%)	1639 (40.5%)	34 (77.3%)	19 (82.6%)
Urinary incontinence	321 (51.3%)	146 (36.3%)	765 (41%)	407 (30.3%)	2980 (46.3%)	1662 (27.8%)	62 (20.1%)	9 (3.8%)	1312 (28.7%)	751 (18.5%)	11 (25%)	5 (21.7%)
Weight loss & anorexia	179 (28.6%)	141 (35.1%)	315 (16.9%)	247 (18.4%)	624 (9.7%)	766 (12.8%)	NA (NA%)	NA (NA%)	564 (12.3%)	478 (11.8%)	NA (NA%)	NA (NA%)
Disability												
Activity limitation	0 (0%)	0 (0%)	20 (1.1%)	8 (0.6%)	642 (10%)	551 (9.2%)	NA (NA%)	0 (0%)	NA (NA%)	0 (0%)	0 (0%)	0 (0%)
Hearing impairment	116 (18.5%)	101 (25.1%)	466 (25%)	457 (34%)	1569 (24.4%)	1626 (27.2%)	112 (36.2%)	100 (42.7%)	726 (15.9%)	871 (21.5%)	NA (NA%)	0 (0%)
Housebound	0 (0%)	0 (0%)	148 (7.9%)	63 (4.7%)	981 (15.2%)	739 (12.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	0 (0%)	199 (10.7%)	129 (9.6%)	176 (2.7%)	152 (2.5%)	NA (NA%)	0 (0%)	197 (4.3%)	177 (4.4%)	0 (0%)	0 (0%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Requiring care	0 (0%)	0 (0%)	134 (7.2%)	73 (5.4%)	922 (14.3%)	649 (10.9%)	0 (0%)	0 (0%)	177 (3.9%)	150 (3.7%)	0 (0%)	0 (0%)
Social vulnerability	201 (32.1%)	123 (30.6%)	103 (5.5%)	70 (5.2%)	1877 (29.1%)	811 (13.6%)	NA (NA%)	0 (0%)	26 (0.6%)	21 (0.5%)	NA (NA%)	0 (0%)
Visual impairment	310 (49.5%)	204 (50.7%)	689 (36.9%)	514 (38.2%)	4334 (67.3%)	3881 (65%)	220 (71.2%)	156 (66.7%)	1629 (35.7%)	1546 (38.2%)	7 (15.9%)	NA (NA%)
Abnormal laboratory value												
Anaemia	211 (33.7%)	163 (40.5%)	626 (33.5%)	413 (30.7%)	3277 (50.9%)	3318 (55.6%)	99 (32%)	61 (26.1%)	1727 (37.8%)	1600 (39.5%)	12 (27.3%)	8 (34.8%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 14. Conditions of Individuals with Severe Frailty by Sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Disease State												
Arthritis	25 (31.2%)	13 (31.7%)	151 (37.2%)	87 (40.1%)	595 (21.8%)	371 (19.8%)	76 (64.4%)	34 (72.3%)	719 (46.8%)	469 (44.1%)	NA (NA%)	NA (NA%)
Atrial fibrillation	35 (43.8%)	23 (56.1%)	142 (35%)	97 (44.7%)	1166 (42.8%)	972 (51.8%)	0 (0%)	0 (0%)	398 (25.9%)	336 (31.6%)	NA (NA%)	NA (NA%)
Chronic kidney disease	71 (88.8%)	38 (92.7%)	381 (93.8%)	191 (88%)	2548 (93.5%)	1750 (93.2%)	115 (97.5%)	43 (91.5%)	1446 (94.1%)	992 (93.3%)	NA (NA%)	NA (NA%)
Cerebrovascular disease	42 (52.5%)	18 (43.9%)	124 (30.5%)	82 (37.8%)	597 (21.9%)	603 (32.1%)	62 (52.5%)	30 (63.8%)	727 (47.3%)	570 (53.6%)	NA (NA%)	NA (NA%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Diabetes	47 (58.8%)	24 (58.5%)	172 (42.4%)	123 (56.7%)	1366 (50.1%)	1164 (62%)	63 (53.4%)	23 (48.9%)	924 (60.2%)	708 (66.6%)	NA (NA%)	NA (NA%)
Foot problems	0 (0%)	0 (0%)	166 (40.9%)	106 (48.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA (NA%)	NA (NA%)
Fragility fracture	32 (40%)	14 (34.1%)	204 (50.2%)	74 (34.1%)	1419 (52.1%)	653 (34.8%)	62 (52.5%)	29 (61.7%)	761 (49.5%)	335 (31.5%)	NA (NA%)	NA (NA%)
Heart failure	37 (46.2%)	18 (43.9%)	83 (20.4%)	64 (29.5%)	1471 (54%)	1172 (62.4%)	103 (87.3%)	42 (89.4%)	937 (61%)	705 (66.3%)	NA (NA%)	NA (NA%)
Heart valve disease	14 (17.5%)	12 (29.3%)	82 (20.2%)	50 (23%)	1032 (37.9%)	777 (41.4%)	26 (22%)	12 (25.5%)	476 (31%)	366 (34.4%)	NA (NA%)	NA (NA%)
Hypertension	63 (78.8%)	24 (58.5%)	270 (66.5%)	124 (57.1%)	2411 (88.5%)	1678 (89.4%)	111 (94.1%)	41 (87.2%)	1469 (95.6%)	1033 (97.2%)	NA (NA%)	NA (NA%)
Hypotension	30 (37.5%)	20 (48.8%)	134 (33%)	76 (35%)	305 (11.2%)	361 (19.2%)	NA (NA%)	6 (12.8%)	273 (17.8%)	210 (19.8%)	NA (NA%)	NA (NA%)
Ischaemic heart disease	35 (43.8%)	21 (51.2%)	155 (38.2%)	124 (57.1%)	703 (25.8%)	865 (46.1%)	92 (78%)	42 (89.4%)	1004 (65.4%)	817 (76.9%)	NA (NA%)	NA (NA%)
Osteoporosis	24 (30%)	7 (17.1%)	139 (34.2%)	29 (13.4%)	1212 (44.5%)	243 (12.9%)	46 (39%)	6 (12.8%)	806 (52.5%)	222 (20.9%)	NA (NA%)	NA (NA%)
Parkinsonism & tremor	NA (NA%)	NA (NA%)	93 (22.9%)	46 (21.2%)	543 (19.9%)	362 (19.3%)	26 (22%)	8 (17%)	435 (28.3%)	283 (26.6%)	NA (NA%)	NA (NA%)
Peptic ulcer	NA (NA%)	NA (NA%)	20 (4.9%)	25 (11.5%)	149 (5.5%)	199 (10.6%)	56 (47.5%)	28 (59.6%)	283 (18.4%)	211 (19.8%)	NA (NA%)	NA (NA%)
Peripheral vascular disease	26 (32.5%)	12 (29.3%)	53 (13.1%)	47 (21.7%)	335 (12.3%)	654 (34.8%)	29 (24.6%)	23 (48.9%)	571 (37.2%)	535 (50.3%)	NA (NA%)	NA (NA%)
Respiratory disease	42 (52.5%)	18 (43.9%)	266 (65.5%)	139 (64.1%)	1062 (39%)	1153 (61.4%)	91 (77.1%)	38 (80.9%)	1055 (68.7%)	812 (76.4%)	NA (NA%)	NA (NA%)
Skin ulcer	26 (32.5%)	10 (24.4%)	32 (7.9%)	31 (14.3%)	522 (19.2%)	419 (22.3%)	10 (8.5%)	5 (10.6%)	309 (20.1%)	208 (19.6%)	NA (NA%)	NA (NA%)
Thyroid disease	26 (32.5%)	10 (24.4%)	151 (37.2%)	31 (14.3%)	1040 (38.2%)	350 (18.6%)	89 (75.4%)	14 (29.8%)	1123 (73.1%)	634 (59.6%)	NA (NA%)	NA (NA%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Urinary system disease	55 (68.8%)	24 (58.5%)	284 (70%)	110 (50.7%)	2140 (78.5%)	1122 (59.7%)	77 (65.3%)	18 (38.3%)	1072 (69.8%)	506 (47.6%)	NA (NA%)	NA (NA%)
Symptoms/Signs												
Dyspnoea	55 (68.8%)	27 (65.9%)	336 (82.8%)	183 (84.3%)	1081 (39.7%)	687 (36.6%)	6 (5.1%)	0 (0%)	636 (41.4%)	465 (43.7%)	NA (NA%)	NA (NA%)
Dizziness	35 (43.8%)	23 (56.1%)	261 (64.3%)	141 (65%)	1318 (48.4%)	776 (41.3%)	46 (39%)	21 (44.7%)	1002 (65.2%)	596 (56.1%)	NA (NA%)	NA (NA%)
Falls	0 (0%)	0 (0%)	270 (66.5%)	110 (50.7%)	944 (34.6%)	483 (25.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA (NA%)	NA (NA%)
Memory & Cognitive problems	33 (41.2%)	18 (43.9%)	138 (34%)	63 (29%)	1301 (47.7%)	801 (42.7%)	17 (14.4%)	10 (21.3%)	511 (33.3%)	353 (33.2%)	NA (NA%)	NA (NA%)
Sleep disturbance	42 (52.5%)	22 (53.7%)	217 (53.4%)	108 (49.8%)	1317 (48.3%)	940 (50.1%)	99 (83.9%)	42 (89.4%)	871 (56.7%)	598 (56.3%)	NA (NA%)	NA (NA%)
Urinary incontinence	56 (70%)	20 (48.8%)	246 (60.6%)	99 (45.6%)	2016 (74%)	1019 (54.3%)	47 (39.8%)	NA (NA%)	769 (50.1%)	379 (35.7%)	NA (NA%)	NA (NA%)
Weight loss & anorexia	33 (41.2%)	20 (48.8%)	136 (33.5%)	69 (31.8%)	431 (15.8%)	367 (19.5%)	7 (5.9%)	NA (NA%)	368 (24%)	247 (23.2%)	NA (NA%)	NA (NA%)
Disability												
Activity limitation	0 (0%)	0 (0%)	5 (1.2%)	NA (NA%)	387 (14.2%)	316 (16.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA (NA%)	NA (NA%)
Hearing impairment	28 (35%)	14 (34.1%)	157 (38.7%)	96 (44.2%)	959 (35.2%)	652 (34.7%)	49 (41.5%)	26 (55.3%)	481 (31.3%)	411 (38.7%)	NA (NA%)	NA (NA%)
Housebound	0 (0%)	0 (0%)	57 (14%)	28 (12.9%)	1095 (40.2%)	679 (36.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA (NA%)	NA (NA%)
Mobility transfer	0 (0%)	0 (0%)	107 (26.4%)	40 (18.4%)	215 (7.9%)	159 (8.5%)	0 (0%)	0 (0%)	128 (8.3%)	116 (10.9%)	NA (NA%)	NA (NA%)
Requiring care	0 (0%)	0 (0%)	71 (17.5%)	23 (10.6%)	1014 (37.2%)	579 (30.8%)	0 (0%)	0 (0%)	105 (6.8%)	76 (7.1%)	NA (NA%)	NA (NA%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Social vulnerability	44 (55%)	24 (58.5%)	44 (10.8%)	17 (7.8%)	1140 (41.8%)	453 (24.1%)	NA (NA%)	0 (0%)	17 (1.1%)	NA (NA%)	NA (NA%)	NA (NA%)
Visual impairment	53 (66.2%)	27 (65.9%)	221 (54.4%)	114 (52.5%)	2163 (79.4%)	1435 (76.4%)	105 (89%)	41 (87.2%)	890 (57.9%)	599 (56.3%)	NA (NA%)	NA (NA%)
Abnormal laboratory value												
Anaemia	52 (65%)	24 (58.5%)	195 (48%)	115 (53%)	1952 (71.6%)	1423 (75.8%)	67 (56.8%)	28 (59.6%)	910 (59.2%)	657 (61.8%)	NA (NA%)	NA (NA%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 15 Characteristics of Polypharmacy (using >=5 drugs threshold) by sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Median Age	72	73	72	74	74	74	69	70	75	74	70	72
Age Group: 18 to 44	105 (2%)	21 (0.4%)	359 (2.4%)	122 (0.8%)	864 (3.1%)	405 (1.2%)	27 (4.5%)	13 (2%)	261 (1.8%)	128 (0.8%)	37 (5.6%)	17 (2.7%)
Age Group: 45 to 64	1256 (24.1%)	979 (18%)	3793 (25.4%)	2578 (17.2%)	6751 (24.4%)	6397 (19.7%)	176 (29.5%)	175 (26.3%)	2932 (20.8%)	3228 (20.4%)	196 (29.8%)	132 (20.9%)
Age Group: 65 to 74	1717 (33%)	1994 (36.7%)	4350 (29.2%)	5389 (36%)	6827 (24.6%)	10620 (32.7%)	214 (35.8%)	267 (40.1%)	3481 (24.6%)	4936 (31.2%)	190 (28.9%)	201 (31.9%)
Age Group: 75 to 84	1513 (29.1%)	1870 (34.4%)	4374 (29.3%)	5144 (34.3%)	7876 (28.4%)	10314 (31.8%)	138 (23.1%)	179 (26.9%)	4967 (35.2%)	5756 (36.4%)	169 (25.7%)	206 (32.6%)
Age Group: 85 to 120	616 (11.8%)	574 (10.6%)	2046 (13.7%)	1750 (11.7%)	5394 (19.5%)	4699 (14.5%)	42 (7%)	32 (4.8%)	2481 (17.6%)	1784 (11.3%)	65 (9.9%)	75 (11.9%)

Sex: Female	5207 (100%)	0 (0%)	14922 (100%)	0 (0%)	27715 (100%)	0 (0%)	597 (100%)	0 (0%)	14122 (100%)	0 (0%)	657 (100%)	0 (0%)
Sex: Male	0 (0%)	5438 (100%)	0 (0%)	14983 (100%)	0 (0%)	32435 (100%)	0 (0%)	666 (100%)	0 (0%)	15832 (100%)	0 (0%)	631 (100%)
Sex: None	NA	NA	NA	NA	NA	NA	NA	NA	0 (0%)	0 (0%)	NA	NA
Median frailty score	0.111	0.111	0.139	0.111	0.194	0.167	0.25	0.194	0.194	0.167	0.111	0.111
Median number of medications	8	8	9	8	8	9	6	6	7	7	7	7

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5.

Appendix II. Table 16. Conditions among individuals with Polypharmacy (using >=5 drugs threshold) by sex and database.

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Disease State												
Arthritis	522 (10%)	342 (6.3%)	2069 (13.9%)	1939 (12.9%)	4184 (15.1%)	4064 (12.5%)	275 (46.1%)	254 (38.1%)	2764 (19.6%)	2738 (17.3%)	143 (21.8%)	134 (21.2%)
Atrial fibrillation	469 (9%)	632 (11.6%)	1274 (8.5%)	2039 (13.6%)	3482 (12.6%)	5266 (16.2%)	0 (0%)	0 (0%)	1362 (9.6%)	1833 (11.6%)	0 (0%)	0 (0%)
Chronic kidney disease	2422 (46.5%)	1694 (31.2%)	6360 (42.6%)	5280 (35.2%)	16825 (60.7%)	17589 (54.2%)	448 (75%)	371 (55.7%)	7781 (55.1%)	7769 (49.1%)	232 (35.3%)	146 (23.1%)
Cerebrovascular disease	530 (10.2%)	578 (10.6%)	1142 (7.7%)	1473 (9.8%)	1725 (6.2%)	3117 (9.6%)	134 (22.4%)	126 (18.9%)	2450 (17.3%)	3210 (20.3%)	49 (7.5%)	66 (10.5%)
Diabetes	970 (18.6%)	1183 (21.8%)	2524 (16.9%)	3206 (21.4%)	7183 (25.9%)	11633 (35.9%)	170 (28.5%)	210 (31.5%)	4767 (33.8%)	6306 (39.8%)	121 (18.4%)	175 (27.7%)
Foot problems	0 (0%)	0 (0%)	1421 (9.5%)	1483 (9.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Fragility fracture	518 (9.9%)	301 (5.5%)	2593 (17.4%)	1418 (9.5%)	6061 (21.9%)	3845 (11.9%)	170 (28.5%)	157 (23.6%)	2840 (20.1%)	1898 (12%)	51 (7.8%)	24 (3.8%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Heart failure	344 (6.6%)	397 (7.3%)	527 (3.5%)	856 (5.7%)	3493 (12.6%)	4401 (13.6%)	301 (50.4%)	385 (57.8%)	3116 (22.1%)	3624 (22.9%)	61 (9.3%)	74 (11.7%)
Heart valve disease	171 (3.3%)	207 (3.8%)	601 (4%)	727 (4.9%)	2977 (10.7%)	3732 (11.5%)	41 (6.9%)	58 (8.7%)	1635 (11.6%)	1837 (11.6%)	11 (1.7%)	18 (2.9%)
Hypertension	2089 (40.1%)	2031 (37.3%)	5003 (33.5%)	5473 (36.5%)	15826 (57.1%)	21049 (64.9%)	435 (72.9%)	500 (75.1%)	10889 (77.1%)	12367 (78.1%)	438 (66.7%)	462 (73.2%)
Hypotension	476 (9.1%)	530 (9.7%)	825 (5.5%)	889 (5.9%)	822 (3%)	1259 (3.9%)	13 (2.2%)	11 (1.7%)	786 (5.6%)	663 (4.2%)	23 (3.5%)	23 (3.6%)
Ischaemic heart disease	576 (11.1%)	1067 (19.6%)	1336 (9%)	2727 (18.2%)	2046 (7.4%)	5740 (17.7%)	251 (42%)	358 (53.8%)	3707 (26.2%)	5891 (37.2%)	54 (8.2%)	114 (18.1%)
Osteoporosis	350 (6.7%)	113 (2.1%)	1568 (10.5%)	325 (2.2%)	5972 (21.5%)	1153 (3.6%)	119 (19.9%)	19 (2.9%)	2943 (20.8%)	892 (5.6%)	145 (22.1%)	45 (7.1%)
Parkinsonism & tremor	36 (0.7%)	64 (1.2%)	659 (4.4%)	669 (4.5%)	1798 (6.5%)	2005 (6.2%)	57 (9.5%)	35 (5.3%)	1412 (10%)	1204 (7.6%)	47 (7.2%)	31 (4.9%)
Peptic ulcer	52 (1%)	66 (1.2%)	263 (1.8%)	389 (2.6%)	609 (2.2%)	1279 (3.9%)	156 (26.1%)	169 (25.4%)	821 (5.8%)	964 (6.1%)	24 (3.7%)	18 (2.9%)
Peripheral vascular disease	271 (5.2%)	400 (7.4%)	374 (2.5%)	631 (4.2%)	948 (3.4%)	3669 (11.3%)	46 (7.7%)	116 (17.4%)	1933 (13.7%)	3162 (20%)	6 (0.9%)	24 (3.8%)
Respiratory disease	1217 (23.4%)	1182 (21.7%)	4502 (30.2%)	4156 (27.7%)	5765 (20.8%)	10135 (31.2%)	317 (53.1%)	321 (48.2%)	5893 (41.7%)	6414 (40.5%)	273 (41.6%)	321 (50.9%)
Skin ulcer	248 (4.8%)	173 (3.2%)	214 (1.4%)	205 (1.4%)	1269 (4.6%)	1329 (4.1%)	28 (4.7%)	24 (3.6%)	850 (6%)	839 (5.3%)	5 (0.8%)	NA (NA%)
Thyroid disease	484 (9.3%)	168 (3.1%)	2041 (13.7%)	732 (4.9%)	6935 (25%)	2597 (8%)	285 (47.7%)	72 (10.8%)	6805 (48.2%)	4172 (26.4%)	150 (22.8%)	52 (8.2%)
Urinary system disease	1588 (30.5%)	727 (13.4%)	3007 (20.2%)	1488 (9.9%)	12307 (44.4%)	7589 (23.4%)	232 (38.9%)	136 (20.4%)	4559 (32.3%)	2506 (15.8%)	91 (13.9%)	47 (7.4%)
Symptoms/Signs												
Dyspnoea	843 (16.2%)	813 (15%)	4860 (32.6%)	4736 (31.6%)	3895 (14.1%)	3520 (10.9%)	13 (2.2%)	12 (1.8%)	1984 (14%)	1964 (12.4%)	NA (NA%)	NA (NA%)

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Dizziness	720 (13.8%)	597 (11%)	2810 (18.8%)	2222 (14.8%)	7193 (26%)	5690 (17.5%)	105 (17.6%)	73 (11%)	3431 (24.3%)	2680 (16.9%)	63 (9.6%)	41 (6.5%)
Falls	0 (0%)	0 (0%)	2271 (15.2%)	1307 (8.7%)	2811 (10.1%)	1687 (5.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (0.8%)	NA (NA%)
Memory & Cognitive problems	368 (7.1%)	381 (7%)	944 (6.3%)	871 (5.8%)	3960 (14.3%)	3730 (11.5%)	36 (6%)	28 (4.2%)	1647 (11.7%)	1416 (8.9%)	24 (3.7%)	22 (3.5%)
Sleep disturbance	947 (18.2%)	718 (13.2%)	2382 (16%)	1905 (12.7%)	7185 (25.9%)	7625 (23.5%)	307 (51.4%)	286 (42.9%)	3613 (25.6%)	3674 (23.2%)	307 (46.7%)	217 (34.4%)
Urinary incontinence	955 (18.3%)	748 (13.8%)	2497 (16.7%)	1671 (11.2%)	7322 (26.4%)	4129 (12.7%)	102 (17.1%)	10 (1.5%)	2552 (18.1%)	1574 (9.9%)	44 (6.7%)	40 (6.3%)
Weight loss & anorexia	548 (10.5%)	590 (10.8%)	1019 (6.8%)	989 (6.6%)	1806 (6.5%)	2388 (7.4%)	11 (1.8%)	NA (NA%)	1163 (8.2%)	1168 (7.4%)	7 (1.1%)	NA (NA%)
Disability												
Activity limitation	0 (0%)	0 (0%)	30 (0.2%)	23 (0.2%)	1636 (5.9%)	1591 (4.9%)	NA (NA%)	0 (0%)	NA (NA%)	0 (0%)	0 (0%)	0 (0%)
Hearing impairment	381 (7.3%)	497 (9.1%)	1552 (10.4%)	2131 (14.2%)	4261 (15.4%)	5348 (16.5%)	135 (22.6%)	188 (28.2%)	1335 (9.5%)	1679 (10.6%)	6 (0.9%)	6 (1%)
Housebound	0 (0%)	0 (0%)	449 (3%)	232 (1.5%)	2354 (8.5%)	1690 (5.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mobility transfer	0 (0%)	0 (0%)	516 (3.5%)	354 (2.4%)	465 (1.7%)	398 (1.2%)	NA (NA%)	0 (0%)	362 (2.6%)	299 (1.9%)	0 (0%)	0 (0%)
Requiring care	0 (0%)	0 (0%)	500 (3.4%)	300 (2%)	2256 (8.1%)	1584 (4.9%)	0 (0%)	0 (0%)	346 (2.5%)	295 (1.9%)	0 (0%)	0 (0%)
Social vulnerability	549 (10.5%)	468 (8.6%)	314 (2.1%)	218 (1.5%)	4736 (17.1%)	2224 (6.9%)	5 (0.8%)	0 (0%)	56 (0.4%)	25 (0.2%)	5 (0.8%)	6 (1%)
Visual impairment	1120 (21.5%)	1153 (21.2%)	2423 (16.2%)	2392 (16%)	12945 (46.7%)	14220 (43.8%)	326 (54.6%)	310 (46.5%)	3059 (21.7%)	3031 (19.1%)	55 (8.4%)	54 (8.6%)
Abnormal laboratory value												

Variable	IPCI		CPRD GOLD		SIDIAP		EBB		IQVIA DA Germany		IQVIA LPD Belgium	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Anaemia	742 (14.3%)	741 (13.6%)	2108 (14.1%)	1744 (11.6%)	9412 (34%)	9461 (29.2%)	203 (34%)	134 (20.1%)	3493 (24.7%)	3552 (22.4%)	63 (9.6%)	71 (11.3%)

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 17 One-year hospitalisations rate by sex.

Database	Hospitalisations Rate	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
SIDIAP	Females	1.16	1.39	1.45	1.45	1.36	1.43
	Males	1.20	1.39	1.59	1.67	1.37	1.48
EBB	Females	3.66	3.79	3.85	3.60	3.94	4.57
	Males	3.00	2.97	2.51	4.03	3.05	3.43

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 18 One-year mortality risk by sex.

Database	Mortality Risk	FIT	MILD	MODERATE	SEVERE	Polypharmacy >=5	Polypharmacy >=10
IPCI	Females	0.21	0.37	0.47	0.57	0.37	0.46
	Males	0.29	0.45	0.57	0.58	0.42	0.50
CPRD GOLD	Females	0.22	0.40	0.49	0.57	0.40	0.50

	Males	0.27	0.44	0.56	0.56	0.43	0.53
SIDIAP	Females	0.16	0.31	0.51	0.69	0.37	0.47
	Males	0.27	0.42	0.62	0.77	0.45	0.54
EBB	Females	0.12	0.17	0.26	0.27	0.24	0.26
	Males	0.15	0.21	0.26	0.58	0.25	0.31

All values are N (%) unless otherwise stated. FI, frailty index. FI scores of 0–0.12 = fit; >0.12–0.24 = mild frailty; >0.24–0.36 = moderate frailty; >0.36 = severe frailty. Polypharmacy was defined as >= 5 or >= 10 medications (ingredient level, maximum number of drug eras that overlap on any day during the 90-day period before the index date). NA=Count s<5. SIDIAP and EBB = databases with hospital/registry linkage.

Appendix II. Table 19. Demographic characteristics and median frailty score by cancer type in each database.

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
Solid tumors							
Breast Cancer	Median Age	61	63	60	58	64	62
	Age Group: 18 to 44	613 (10.8%)	1220 (8.6%)	3241 (13.4%)	66 (13.3%)	3664 (8.3%)	134 (12.7%)
	Age Group: 45 to 64	2669 (47%)	6573 (46.2%)	11674 (48.1%)	262 (52.9%)	18852 (42.7%)	444 (42.1%)
	Age Group: 65 to 74	1406 (24.7%)	3372 (23.7%)	4346 (17.9%)	115 (23.2%)	10178 (23%)	252 (23.9%)
	Age Group: 75 to 84	676 (11.9%)	2106 (14.8%)	3066 (12.6%)	45 (9.1%)	8991 (20.3%)	165 (15.7%)
	Age Group: 85 to 120	317 (5.6%)	945 (6.6%)	1918 (7.9%)	7 (1.4%)	2511 (5.7%)	59 (5.6%)
	sex: Female	5649 (99.4%)	14213 (100%)	24039 (99.1%)	494 (99.8%)	43444 (98.3%)	952 (90.3%)
	sex: Male	32 (0.6%)	NA (NA%)	207 (0.9%)	NA (NA%)	719 (1.6%)	102 (9.7%)
	sex: None					33 (0.1%)	

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
	Median frailty score	0.056	0.056	0.083	0.111	0.028	0.056
	Frailty Category: Fit	4640 (81.7%)	10863 (76.4%)	16293 (67.2%)	259 (52.3%)	36797 (83.3%)	838 (79.5%)
	Frailty Category: Mild	865 (15.2%)	2556 (18%)	5332 (22%)	173 (34.9%)	5366 (12.1%)	197 (18.7%)
	Frailty Category: Moderate	164 (2.9%)	652 (4.6%)	1867 (7.7%)	52 (10.5%)	1572 (3.6%)	17 (1.6%)
	Frailty Category: Severe	12 (0.2%)	145 (1%)	754 (3.1%)	11 (2.2%)	461 (1%)	NA (NA%)
Colorectal Cancer	Median Age	71	71	72	68	71	70
	Age Group: 18 to 44	128 (2.7%)	372 (3.9%)	710 (2.8%)	31 (4.6%)	811 (3.9%)	21 (6.8%)
	Age Group: 45 to 64	1466 (30.4%)	2667 (27.6%)	7174 (28.7%)	223 (33.4%)	6120 (29.5%)	96 (31.3%)
	Age Group: 65 to 74	1526 (31.6%)	2919 (30.2%)	6571 (26.3%)	218 (32.6%)	5417 (26.1%)	70 (22.8%)
	Age Group: 75 to 84	1279 (26.5%)	2544 (26.3%)	6744 (27%)	152 (22.8%)	6325 (30.5%)	71 (23.1%)
	Age Group: 85 to 120	426 (8.8%)	1154 (12%)	3782 (15.1%)	44 (6.6%)	2082 (10%)	49 (16%)
	sex: Female	2175 (45.1%)	4341 (45%)	10547 (42.2%)	416 (62.3%)	10067 (48.5%)	155 (50.5%)
	sex: Male	2650 (54.9%)	5315 (55%)	14434 (57.8%)	252 (37.7%)	10668 (51.4%)	152 (49.5%)
	sex: None					20 (0.1%)	
	Median frailty score	0.056	0.083	0.139	0.167	0.056	0.083
	Frailty Category: Fit	3644 (75.5%)	6546 (67.8%)	12254 (49.1%)	220 (32.9%)	14402 (69.4%)	234 (76.2%)
	Frailty Category: Mild	937 (19.4%)	2364 (24.5%)	7757 (31.1%)	250 (37.4%)	4358 (21%)	65 (21.2%)
	Frailty Category: Moderate	214 (4.4%)	637 (6.6%)	3580 (14.3%)	144 (21.6%)	1491 (7.2%)	6 (2%)

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
	Frailty Category: Severe	30 (0.6%)	109 (1.1%)	1390 (5.6%)	54 (8.1%)	504 (2.4%)	NA (NA%)
Endometrial	Median Age	70	67	66	60	66	74
	Age Group: 18 to 44	11 (2%)	41 (2.8%)	175 (5.5%)	12 (9.3%)	159 (8.5%)	NA (NA%)
	Age Group: 45 to 64	169 (30.3%)	565 (38.1%)	1287 (40.6%)	71 (55%)	727 (38.8%)	7 (15.6%)
	Age Group: 65 to 74	205 (36.8%)	485 (32.7%)	884 (27.9%)	30 (23.3%)	451 (24.1%)	13 (28.9%)
	Age Group: 75 to 84	141 (25.3%)	307 (20.7%)	570 (18%)	15 (11.6%)	422 (22.5%)	17 (37.8%)
	Age Group: 85 to 120	31 (5.6%)	83 (5.6%)	254 (8%)	NA (NA%)	115 (6.1%)	5 (11.1%)
	sex: Female	557 (100%)	1481 (100%)	3170 (100%)	129 (100%)	1868 (99.7%)	42 (93.3%)
	sex: Male			NA (NA%)		5 (0.3%)	NA (NA%)
	sex: None					NA (NA%)	
	Median frailty score	0.083	0.083	0.111	0.139	0.056	0.111
	Frailty Category: Fit	430 (77.2%)	1067 (72%)	1684 (53.1%)	55 (42.6%)	1434 (76.5%)	30 (66.7%)
	Frailty Category: Mild	106 (19%)	334 (22.6%)	995 (31.4%)	52 (40.3%)	307 (16.4%)	13 (28.9%)
	Frailty Category: Moderate	20 (3.6%)	69 (4.7%)	370 (11.7%)	19 (14.7%)	93 (5%)	NA (NA%)
	Frailty Category: Severe	NA (NA%)	11 (0.7%)	122 (3.8%)	NA (NA%)	40 (2.1%)	
Lung Cancer	Median Age	70	73	68	68	69	67
	Age Group: 18 to 44	110 (2.1%)	60 (0.8%)	250 (2%)	NA (NA%)	384 (2.3%)	41 (10.9%)
	Age Group: 45 to 64	1490 (28.6%)	1496 (20.8%)	4450 (36.4%)	72 (35.5%)	5341 (32.3%)	124 (33%)

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
	Age Group: 65 to 74	1867 (35.9%)	2590 (36%)	3819 (31.3%)	77 (37.9%)	5506 (33.3%)	115 (30.6%)
	Age Group: 75 to 84	1347 (25.9%)	2306 (32%)	2584 (21.1%)	45 (22.2%)	4330 (26.2%)	69 (18.4%)
	Age Group: 85 to 120	393 (7.5%)	744 (10.3%)	1117 (9.1%)	7 (3.4%)	967 (5.9%)	27 (7.2%)
	sex: Female	2340 (44.9%)	3647 (50.7%)	3515 (28.8%)	88 (43.3%)	7123 (43.1%)	152 (40.4%)
	sex: Male	2867 (55.1%)	3549 (49.3%)	8705 (71.2%)	115 (56.7%)	9392 (56.8%)	224 (59.6%)
	sex: None					13 (0.1%)	
	Median frailty score	0.083	0.111	0.139	0.167	0.083	0.083
	Frailty Category: Fit	3452 (66.3%)	3782 (52.6%)	5981 (48.9%)	60 (29.6%)	10766 (65.1%)	258 (68.6%)
	Frailty Category: Mild	1359 (26.1%)	2449 (34%)	4043 (33.1%)	84 (41.4%)	3851 (23.3%)	105 (27.9%)
	Frailty Category: Moderate	349 (6.7%)	792 (11%)	1634 (13.4%)	47 (23.2%)	1466 (8.9%)	13 (3.5%)
	Frailty Category: Severe	47 (0.9%)	173 (2.4%)	562 (4.6%)	12 (5.9%)	445 (2.7%)	
Ovarian Cancer	Median Age	67	66	61	57	62	64
	Age Group: 18 to 44	29 (6.8%)	117 (8.3%)	387 (13.6%)	43 (21.9%)	622 (14.3%)	7 (17.1%)
	Age Group: 45 to 64	165 (38.5%)	546 (38.5%)	1259 (44.3%)	95 (48.5%)	1774 (40.7%)	14 (34.1%)
	Age Group: 65 to 74	126 (29.4%)	368 (26%)	563 (19.8%)	37 (18.9%)	919 (21.1%)	9 (22%)
	Age Group: 75 to 84	84 (19.6%)	294 (20.7%)	398 (14%)	16 (8.2%)	832 (19.1%)	6 (14.6%)
	Age Group: 85 to 120	25 (5.8%)	92 (6.5%)	236 (8.3%)	5 (2.6%)	211 (4.8%)	5 (12.2%)
	sex: Female	429 (100%)	1416 (99.9%)	2843 (100%)	196 (100%)	4110 (94.3%)	32 (78%)

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
	sex: Male		NA (NA%)	NA (NA%)		247 (5.7%)	9 (22%)
	sex: None					NA (NA%)	
	Median frailty score	0.056	0.056	0.111	0.139	0.056	0.083
	Frailty Category: Fit	332 (77.4%)	1045 (73.7%)	1720 (60.5%)	93 (47.4%)	3335 (76.5%)	29 (70.7%)
	Frailty Category: Mild	76 (17.7%)	308 (21.7%)	751 (26.4%)	73 (37.2%)	718 (16.5%)	8 (19.5%)
	Frailty Category: Moderate	18 (4.2%)	50 (3.5%)	270 (9.5%)	18 (9.2%)	234 (5.4%)	NA (NA%)
	Frailty Category: Severe	NA (NA%)	14 (1%)	103 (3.6%)	12 (6.1%)	71 (1.6%)	NA (NA%)
Pancreatic Cancer	Median Age	71	73	72	68	72	71.5
	Age Group: 18 to 44	25 (2.1%)	27 (1.4%)	152 (2.6%)	9 (5%)	120 (2.1%)	NA (NA%)
	Age Group: 45 to 64	321 (27.4%)	459 (24.2%)	1533 (26.4%)	63 (35.2%)	1485 (26.5%)	24 (23.5%)
	Age Group: 65 to 74	369 (31.5%)	586 (30.9%)	1590 (27.4%)	48 (26.8%)	1570 (28%)	39 (38.2%)
	Age Group: 75 to 84	353 (30.1%)	589 (31%)	1535 (26.4%)	45 (25.1%)	1838 (32.8%)	27 (26.5%)
	Age Group: 85 to 120	104 (8.9%)	237 (12.5%)	999 (17.2%)	14 (7.8%)	590 (10.5%)	11 (10.8%)
	sex: Female	588 (50.2%)	940 (49.5%)	2907 (50%)	111 (62%)	2773 (49.5%)	63 (61.8%)
	sex: Male	584 (49.8%)	958 (50.5%)	2902 (50%)	68 (38%)	2824 (50.4%)	39 (38.2%)
	sex: None					6 (0.1%)	
	Median frailty score	0.083	0.111	0.167	0.167	0.111	0.111
	Frailty Category: Fit	798 (68.1%)	1128 (59.4%)	2309 (39.7%)	57 (31.8%)	3259 (58.2%)	66 (64.7%)

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
	Frailty Category: Mild	295 (25.2%)	596 (31.4%)	2029 (34.9%)	66 (36.9%)	1524 (27.2%)	31 (30.4%)
	Frailty Category: Moderate	68 (5.8%)	142 (7.5%)	1016 (17.5%)	36 (20.1%)	583 (10.4%)	5 (4.9%)
	Frailty Category: Severe	11 (0.9%)	32 (1.7%)	455 (7.8%)	20 (11.2%)	237 (4.2%)	
Prostate	Median Age	71	71	71	67	72	74
	Age Group: 18 to 44	12 (0.3%)	23 (0.2%)	29 (0.2%)	7 (0.7%)	273 (0.6%)	17 (2.2%)
	Age Group: 45 to 64	932 (23.5%)	2961 (23.2%)	4697 (24.3%)	368 (39.3%)	11047 (25.3%)	125 (16.5%)
	Age Group: 65 to 74	1737 (43.7%)	5290 (41.5%)	7330 (38%)	361 (38.6%)	14426 (33%)	257 (33.9%)
	Age Group: 75 to 84	1044 (26.3%)	3524 (27.7%)	5216 (27%)	177 (18.9%)	14703 (33.6%)	248 (32.8%)
	Age Group: 85 to 120	249 (6.3%)	942 (7.4%)	2039 (10.6%)	23 (2.5%)	3268 (7.5%)	110 (14.5%)
	sex: Female	NA (NA%)	NA (NA%)	NA (NA%)	NA (NA%)	303 (0.7%)	17 (2.2%)
	sex: Male	3973 (100%)	12736 (100%)	19308 (100%)	933 (99.7%)	43397 (99.3%)	740 (97.8%)
	sex: None					17 (0%)	
	Median frailty score	0.056	0.083	0.111	0.139	0.056	0.083
	Frailty Category: Fit	3144 (79.1%)	9313 (73.1%)	10981 (56.9%)	425 (45.4%)	35097 (80.3%)	561 (74.1%)
	Frailty Category: Mild	726 (18.3%)	2812 (22.1%)	5957 (30.8%)	362 (38.7%)	6365 (14.6%)	182 (24%)
	Frailty Category: Moderate	94 (2.4%)	538 (4.2%)	1817 (9.4%)	131 (14%)	1816 (4.2%)	14 (1.8%)

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
	Frailty Category: Severe	10 (0.3%)	77 (0.6%)	556 (2.9%)	18 (1.9%)	439 (1%)	
Blood tumors							
Leukaemia	Median Age	70	70	72	68	69	72.5
	Age Group: 18 to 44	69 (6.7%)	181 (7.7%)	422 (8.3%)	26 (12.9%)	729 (9.9%)	10 (7.1%)
	Age Group: 45 to 64	290 (28.2%)	638 (27.3%)	1334 (26.1%)	66 (32.7%)	2075 (28.3%)	35 (25%)
	Age Group: 65 to 74	306 (29.7%)	678 (29%)	1204 (23.6%)	64 (31.7%)	1801 (24.5%)	35 (25%)
	Age Group: 75 to 84	252 (24.5%)	595 (25.5%)	1344 (26.3%)	37 (18.3%)	2111 (28.7%)	44 (31.4%)
	Age Group: 85 to 120	111 (10.8%)	244 (10.4%)	799 (15.6%)	9 (4.5%)	629 (8.6%)	16 (11.4%)
	sex: Female	401 (39%)	954 (40.8%)	2370 (46.4%)	107 (53%)	3405 (46.4%)	65 (46.4%)
	sex: Male	628 (61%)	1382 (59.2%)	2738 (53.6%)	95 (47%)	3937 (53.6%)	75 (53.6%)
	sex: None					NA (NA%)	
	Median frailty score	0.083	0.083	0.139	0.139	0.056	0.083
	Frailty Category: Fit	751 (73%)	1618 (69.3%)	2513 (49.2%)	86 (42.6%)	5436 (74%)	100 (71.4%)
	Frailty Category: Mild	236 (22.9%)	547 (23.4%)	1542 (30.2%)	56 (27.7%)	1329 (18.1%)	35 (25%)
	Frailty Category: Moderate	38 (3.7%)	140 (6%)	761 (14.9%)	44 (21.8%)	444 (6%)	5 (3.6%)
	Frailty Category: Severe	NA (NA%)	31 (1.3%)	292 (5.7%)	16 (7.9%)	136 (1.9%)	
Lymphoma	Median Age	67	67	55	58	65	70.5
	Age Group: 18 to 44	138 (12.5%)	324 (13.6%)	1906 (26.3%)	64 (29.8%)	1663 (15.1%)	17 (17%)

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
	Age Group: 45 to 64	346 (31.4%)	741 (31.1%)	3172 (43.7%)	72 (33.5%)	3709 (33.6%)	22 (22%)
	Age Group: 65 to 74	299 (27.1%)	637 (26.7%)	1015 (14%)	42 (19.5%)	2470 (22.4%)	22 (22%)
	Age Group: 75 to 84	254 (23%)	505 (21.2%)	830 (11.4%)	23 (10.7%)	2523 (22.9%)	24 (24%)
	Age Group: 85 to 120	64 (5.8%)	179 (7.5%)	324 (4.5%)	14 (6.5%)	675 (6.1%)	15 (15%)
	sex: Female	501 (45.5%)	1089 (45.6%)	2712 (37.4%)	140 (65.1%)	5558 (50.3%)	49 (49%)
	sex: Male	601 (54.5%)	1297 (54.4%)	4546 (62.6%)	75 (34.9%)	5478 (49.6%)	51 (51%)
	sex: None					NA (NA%)	
	Median frailty score	0.056	0.056	0.083	0.139	0.056	0.083
	Frailty Category: Fit	868 (78.8%)	1722 (72.2%)	4443 (61.2%)	103 (47.9%)	8529 (77.3%)	81 (81%)
	Frailty Category: Mild	193 (17.5%)	533 (22.3%)	1951 (26.9%)	74 (34.4%)	1743 (15.8%)	18 (18%)
	Frailty Category: Moderate	40 (3.6%)	116 (4.9%)	665 (9.2%)	28 (13%)	597 (5.4%)	NA (NA%)
	Frailty Category: Severe	NA (NA%)	15 (0.6%)	199 (2.7%)	10 (4.7%)	171 (1.5%)	
Multiple Myeloma	Median Age	72	72	73	69.5	72	70
	Age Group: 18 to 44	7 (1.5%)	20 (1.7%)	62 (2.5%)	5 (5.3%)	143 (3.7%)	NA (NA%)
	Age Group: 45 to 64	109 (23.9%)	313 (26.7%)	681 (27%)	32 (34%)	1033 (26.9%)	18 (30%)
	Age Group: 65 to 74	164 (36%)	355 (30.3%)	651 (25.8%)	33 (35.1%)	1056 (27.5%)	21 (35%)
	Age Group: 75 to 84	129 (28.3%)	354 (30.2%)	730 (28.9%)	18 (19.1%)	1294 (33.7%)	14 (23.3%)
	Age Group: 85 to 120	47 (10.3%)	130 (11.1%)	398 (15.8%)	6 (6.4%)	311 (8.1%)	NA (NA%)
	Sex: Female	195 (42.8%)	491 (41.9%)	1258 (49.9%)	56 (59.6%)	1922 (50.1%)	33 (55%)

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
	Sex: Male	261 (57.2%)	681 (58.1%)	1264 (50.1%)	38 (40.4%)	1913 (49.9%)	27 (45%)
	Sex: None					NA (NA%)	
	Median frailty score	0.083	0.083	0.167	0.194	0.083	0.111
	Frailty Category: Fit	321 (70.4%)	731 (62.4%)	970 (38.5%)	24 (25.5%)	2437 (63.5%)	35 (58.3%)
	Frailty Category: Mild	108 (23.7%)	345 (29.4%)	856 (33.9%)	34 (36.2%)	904 (23.6%)	24 (40%)
	Frailty Category: Moderate	24 (5.3%)	79 (6.7%)	498 (19.7%)	27 (28.7%)	384 (10%)	NA (NA%)
	Frailty Category: Severe	NA (NA%)	17 (1.5%)	198 (7.9%)	9 (9.6%)	112 (2.9%)	

All values are N (%) unless otherwise stated. NA=Count <5.

Appendix II. Table 20 Distribution of cancer types by database in older adults (aged >=65).

Cancer type	IPCI	IPCI	CPRD GOLD	CPRD GOLD	SIDIAP	SIDIAP	EBB	EBB	IQVIA DA Germany	IQVIA DA Germany	IQVIA LPD Belgium	IQVIA LPD Belgium
	n (15,296)	%	n (35,095)	%	n (62,554)	%	n (1723)	%	n (97,645)	%	n (1809)	%
Breast Cancer	2399	16	6423	18	9330	15	167	10	21680	22	476	26
Colorectal Cancer	3231	21	6617	19	17097	27	414	24	13824	14	190	11
Endometrial	377	2	875	2	1708	3	45	3	988	1	35	2
Lung Cancer	3607	24	5640	16	7520	12	129	7	10803	11	211	12
Ovarian Cancer	235	2	754	2	1197	2	58	3	1962	2	20	1

Cancer type	IPCI	IPCI	CPRD GOLD	CPRD GOLD	SIDIAP	SIDIAP	EBB	EBB	IQVIA DA Germany	IQVIA DA Germany	IQVIA LPD Belgium	IQVIA LPD Belgium
Pancreatic Cancer	826	5	1412	4	4124	7	107	6	3998	4	77	4
Prostate	3030	20	9756	28	14585	23	561	33	32397	33	615	34
Leukaemia	669	4	1517	4	3347	5	110	6	4541	5	95	5
Lymphoma	617	4	1321	4	2169	3	79	5	5668	6	61	3
Multiple Myeloma	340	2	839	2	1779	3	57	3	2661	3	35	2

All values are N (%) unless otherwise stated. Percentage based on overall cancer counts by database. NA=Count <5.

Appendix II. Table 21. Median frailty score by selected cancer types in older adults (aged >=65).

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
Age Group: 65 to 74							
Breast	Median frailty score	0.056	0.083	0.111	0.194	0.056	0.083
colorectal	Median frailty score	0.056	0.083	0.111	0.194	0.056	0.083
endometrium	Median frailty score	0.083	0.083	0.125	0.167	0.056	0.111
lung	Median frailty score	0.083	0.111	0.139	0.194	0.083	0.111
ovarian	Median frailty score	0.083	0.083	0.139	0.194	0.056	0.056
pancreatic	Median frailty score	0.083	0.083	0.139	0.222	0.083	0.111
prostate	Median frailty score	0.056	0.056	0.111	0.167	0.056	0.083

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
Leukaemia	Median frailty score	0.083	0.083	0.111	0.181	0.056	0.083
Lymphoma	Median frailty score	0.056	0.083	0.139	0.194	0.056	0.083
Multiple Myeloma	Median frailty score	0.083	0.083	0.139	0.194	0.083	0.111
Age Group: 75 to 84							
Breast	Median frailty score	0.111	0.111	0.167	0.222	0.056	0.111
colorectal	Median frailty score	0.111	0.111	0.167	0.25	0.083	0.083
endometrium	Median frailty score	0.083	0.111	0.167	0.222	0.083	0.111
lung	Median frailty score	0.111	0.139	0.194	0.25	0.111	0.111
ovarian	Median frailty score	0.083	0.111	0.194	0.236	0.083	0.111
pancreatic	Median frailty score	0.111	0.111	0.194	0.222	0.139	0.111
prostate	Median frailty score	0.083	0.111	0.139	0.194	0.056	0.083
Leukaemia	dian frailty score	0.111	0.111	0.194	0.25	0.083	0.111
Lymphoma	Median frailty score	0.111	0.111	0.194	0.222	0.083	0.083
Multiple Myeloma	Median frailty score	0.111	0.139	0.222	0.306	0.111	0.125
Age Group: 85 to 120							
Breast	Median frailty score	0.139	0.167	0.25	0.139	0.111	0.111

Cancer Type		IPCI	CPRD GOLD	SIDIAP	EBB	IQVIA DA Germany	IQVIA LPD Belgium
colorectal	Median frailty score	0.139	0.139	0.25	0.25	0.139	0.111
endometrium	Median frailty score	0.111	0.167	0.25		0.111	0.111
lung	n frailty score	0.167	0.167	0.25	0.25	0.167	0.139
ovarian	Median frailty score	0.139	0.167	0.278	0.333	0.167	0.278
pancreatic	Median frailty score	0.139	0.167	0.25	0.264	0.194	0.139
prostate	Median frailty score	0.139	0.139	0.222	0.25	0.083	0.111
Leukaemia	Median frailty score	0.139	0.139	0.25	0.306	0.111	0.111
Lymphoma	Median frailty score	0.139	0.139	0.25	0.236	0.111	0.083
Multiple Myeloma	Median frailty score	0.139	0.139	0.278	0.25	0.167	

All values are N (%) unless otherwise stated. Percentage based on overall cancer counts by database. NA=Count <5.