The Impact of Obesity Disease and its Complications in Japan

Results for the Japan Cohort of the Multicountry IMPACT-O Study

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ABSTRACT

Background and objective: Our study aimed to estimate recorded proportions of people with healthy obesity (PwHO) and people with obesity disease (PwOD) in Japan and describe their sociodemographic and clinical characteristics.

Methods: IMPACT-O was a multicountry, retrospective, observational cohort study conducted in 2018-2022. The Japanese obesity cohort comprised adults (≧18 years) with body mass index (BMI) ≧25 kg/m^2 and/or obesity diagnostic codes from the IQVIA Solutions Japan G. K. Claims database with ≧12 months' observation before/after index. PwHO and PwOD were defined as people in the cohort without and with Japan Society for the Study of Obesity (JASSO)-defined obesity-related complications (ORCs), respectively. Demographics, BMI categories, and clinical visits were described for PwHO and PwOD; ORCs were described for PwOD.

Results: There were 68,567 PwHO (72.5% male) and 43,278 PwOD (66.8% male). Among PwHO and PwOD, 66.4% and 57.3%, respectively, had BMI ≧25 to <27 kg/m^2. In the 12 months post index, the median number of clinical visits was 5.0 (PwHO) versus 19.0 (PwOD). Many PwOD (56.4%) had ≧2 JASSO-defined ORCs; the most common ORCs were hypertension (54.9%), type 2 diabetes (39.5%), and dyslipidemia (28.2%). The proportion of PwOD with ≧2 ORCs and the prevalence of both hypertension and type 2 diabetes increased with increasing BMI. Approximately one-third (34.4%) of PwHO developed ≧1 ORC in the 12-month follow-up.

Conclusion: Our results suggest PwOD in Japan experience a disease burden that often includes multiple ORCs and clinical visits, which tends to increase as BMI increases.

Key words: Disease burden, Obesity, Obesity disease, Obesity-related complications, Real-world data

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INTRODUCTION

Obesity is a complex chronic disease defined by excess body fat that can impair health and reduce quality of life[1-3]. World Health Organization (WHO) data indicate that in 2022, approximately 2.5 billion adults (43% of adults worldwide) were overweight (body mass index [BMI] ≧25 kg/m^2) and 890 million (16%) were living with obesity (BMI ≧30 kg/m^2)[1]. The proportion of adults with overweight or obesity has been increasing for several decades, and the disease burden related to high BMI has increased worldwide since 1990[2]. Obesity frequently coexists with complications such as cardiovascular disease, type 2 diabetes (T2D), obstructive sleep apnea (OSA), osteoarthritis, and several types of cancer[3]. Obesity-related health complications are associated with increased mortality risk, with an estimated 5 million deaths globally attributed to high BMI in 2019[1,2,4]. Beyond metabolic and cardiovascular consequences, obesity imposes a substantial burden on healthcare systems globally. Population-based studies from the United States and Europe have consistently demonstrated that increasing BMI is positively associated with greater healthcare resource utilization (HCRU), including outpatient visits, hospitalizations, and emergency department encounters, as well as higher total healthcare costs[5,6].

The relationship between BMI and obesity-related health risks varies across ethnic groups and BMI ranges. In Asian populations, including in Japan, lower BMI cutoffs (≧25 or ≧27.5 kg/m^2) for defining obesity have been recommended, given that these populations have a propensity for central adiposity and metabolic complications at lower BMI levels compared with Western populations[7-11]. In people with obesity disease (PwOD), BMI ≧25.0 kg/m^2 is accompanied by ≧1 of 11 specified obesity-related complications (ORCs) or by the presence of visceral fat obesity[12]. In contrast, people with BMI ≧25.0 kg/m^2 without any obesity-related health problems or visceral fat obesity may be considered as people with "healthy obesity" (PwHO). The concept of "metabolically healthy obesity" (MHO) has gained considerable attention, referring to people with obesity who do not exhibit cardiometabolic abnormalities such as hypertension, dyslipidemia, and insulin resistance[13-16]. However, substantial heterogeneity exists in MHO definitions across studies[13,14], and the notion that MHO represents a benign condition of the disease has been challenged[17], with accumulating evidence suggesting instead that it represents a transient state to unhealthy obesity[15,18]. Notably, studies in Asian populations, including Japanese studies, have indicated that the clinical implications of MHO may differ from those in Western populations due to metabolic risk at lower BMI thresholds[19,20]. These findings suggest that obesity without current metabolic abnormalities should not be considered a risk-free condition, and understanding the characteristics and outcomes of MHO in the Japanese population is clinically important.

In addition to characterizing PwHO, understanding the cumulative ORC burden among PwOD across BMI categories is equally important. Beyond the distinction between metabolically healthy and unhealthy obesity, the accumulation of multiple ORCs (multimorbidity) represents a growing clinical and public health concern[21-23]. Obesity has been identified as a central driver of cardiometabolic disease clustering, with prospective cohort studies demonstrating a dose-response relationship between BMI and the risk of developing complex multimorbidity[22]. The presence of multiple comorbidities has significant prognostic implications. Longitudinal

studies have shown that the accumulation of cardiometabolic diseases is associated with increased mortality risk[21]. Despite this growing body of evidence from Western populations, data on the prevalence and patterns of multiple ORCs in Japanese individuals remain limited. Given the unique obesity definition in Japan and the lower BMI thresholds at which metabolic complications occur in Asian populations, understanding the patterns of ORCs with the burden of multimorbidity across BMI categories among Japanese people with obesity is particularly important for informing clinical practice and health policy in Japan. However, there is a paucity of information currently available about people in Japan with BMI ≧25.0 kg/m^2, including characteristics of people living with obesity, obesity diagnosis recording rates, ORCs, and weight loss treatments.

The epIdeMiology landscape and PAtient Care paThways of Obesity (IMPACT-O) study is a multinational real-world descriptive study of adults with BMI ≧25.0 kg/m^2 in 7 European and Asia-Pacific countries (France, Germany, Italy, Spain, United Kingdom, Australia, and Japan) using data obtained from existing healthcare databases[24]. The IMPACT-O study described that among adults in Japan with ≧1 BMI recording (N=2,082,594), the recorded proportion of obesity was 30.1% when obesity was defined as BMI ≧25 kg/m^2 and 31.5% when obesity was defined by BMI and/or obesity diagnostic codes[24]. Furthermore, >60% of adults in Japan with obesity had ≧1 ORCs. Here we present the results of a further analysis of the Japanese cohort from the IMPACT-O study. The objectives of the present analysis were to estimate the recorded proportions of PwOD and PwHO in Japan between 2018 and 2022; to describe their sociodemographic and clinical characteristics, including ORC types and their prevalences; and to describe the number of ORCs, hospitalizations, and clinical visits across BMI categories, through a 1-year follow-up.

OBJECTIVE AND METHODS

1 Study design

IMPACT-O was a multicountry, retrospective, observational cohort study that used existing healthcare databases. All databases were standardized to the Observational Medical Outcomes Partnership (OMOP) Common Data Model, developed and maintained by the Observational Health Data Sciences and Informatics initiative (https://ohdsi.github.io/CommonDataModel/). The IMPACT-O study period was from January 1, 2018, to December 31, 2022, and the study design has been described previously for the multicountry analysis[24].

Japanese data for IMPACT-O were obtained from the IQVIA Japan Claims database, which includes data from over 6.6 million active participants collected from over 69 employer-sponsored health insurance systems from 2013 to the present. The database includes data from annual health checkups, such as BMI records and results of selected laboratory tests (e.g., HbA1c). Participants in the database represent a diverse cross-section of the Japanese population. IQVIA Japan Claims data from January 1, 2018, to May 31, 2022 (data extraction date: April 2023) were used in the analyses reported in this article.

All analyses performed in this study were in accordance with the data use agreement terms as specified by the data owners. As the data were used under a data use agreement with de-identified records, there was no requirement for registration of the protocol, nor was there a requirement for ethical review by an Institutional Review Board. Informed consent was not required because the study used de-identified data from the IQVIA Japan Claims database.

2 Study population

The Obesity Cohort consisted of all adults with newly identified obesity within the study period (2018–2022) in the IQVIA Japan Claims database. To be included in the Obesity Cohort, patients were adults (≧18 years at index date), had ≧1 BMI measurement ≧25.0 kg/m^2 (extracted from the annual checkup data in the database) and/or diagnostic code of obesity (International Statistical Classification of Diseases and Related Health Problems 10th Revision [ICD-10] codes E66.9, E66.8, or E66.0), and ≧12 months of observation both before and after the index date. The index date was defined as the first record of diagnostic code or BMI measurement indicating obesity. Exclusion criteria for the Obesity Cohort were age or sex missing from the patient record, a BMI record of <25 kg/m^2 within ±30 days of the index date (to avoid contradicting diagnostic code and BMI record), or a BMI record of ≧25 kg/m^2 at any time prior to the index date.

Within the Obesity Cohort, patients who had ≧1 ORCs from the overall ORC set but no JASSO-defined ORC within 1 year prior to the index date were excluded, and the remaining patients were categorized as PwHO or PwOD. PwHO were defined as those who had no ORCs within 1 year prior to the index date using the overall ORC set defined in the multicountry analysis[24]. PwOD were defined as those who had ≧1 JASSO-defined ORC within 1 year prior to the index date. The overall ORC set is listed in **Table S1**, and JASSO-defined ORCs are described in the "Outcome variables" section below.

Additional analyses of the presence of ORCs in the prevalent Japanese study population were performed using the Prevalent Cohort, as described in a section of the Supplementary Information (Prevalent Cohort Methods; Prevalent Cohort Results; **Fig. S3** and **S4**).

3 Outcome variables

1) Demographic and metabolic characteristics

Demographic (sex and age) and BMI characteristics were described for PwHO and PwOD in the Obesity Cohort at the index date (**Fig. 1a**). BMI characteristics included the frequency and percentage distribution of PwHO and PwOD within each of these BMI categories: 25.0 to <27.0 kg/m^2, ≧27.0 to <30.0 kg/m^2, ≧30.0 to <35.0 kg/m^2, ≧35.0 to <40.0 kg/m^2, and ≧40.0 kg/m^2. Among PwOD only, demographic characteristics were also described within each of the BMI categories. Patient metabolic characteristics (glycated hemoglobin [HbA1c], lipid levels, and blood pressure) were described for PwHO and PwOD in the Obesity Cohort at the index date (**Fig. 1a**).

2) ORCs

ORCs were described for the 1-year period prior to the index date (baseline) and the 1-year period after the index date (follow-up) (**Fig. 1a**). Unless otherwise specified, ORCs were identified by ICD-10 diagnosis codes only.

The overall ORC set was defined for the multicountry analysis[24] and is listed in **Table S1**. The JASSO-defined ORCs were hypertension (diagnosis codes and medication codes); dyslipidemia (diagnosis codes and medication codes); T2D (diagnosis codes and medication codes); impaired glucose tolerance (IGT) plus T2D; IGT only; stroke plus transient ischemic attack (TIA); cardiovascular disease (CVD)/myocardial infarction (MI)/angina (a newly added JASSO comorbidity category); OSA; gout, including hyperuricemia; metabolic dysfunction-associated steatotic liver disease (MASLD)/metabolic dysfunction-associated steatohepatitis (MASH); chronic kidney disease; disorder of female reproductive system; and motor dysfunction: arthritis/osteoarthritis (a newly added JASSO comorbidity category)[12]. Given that the definition of diag-

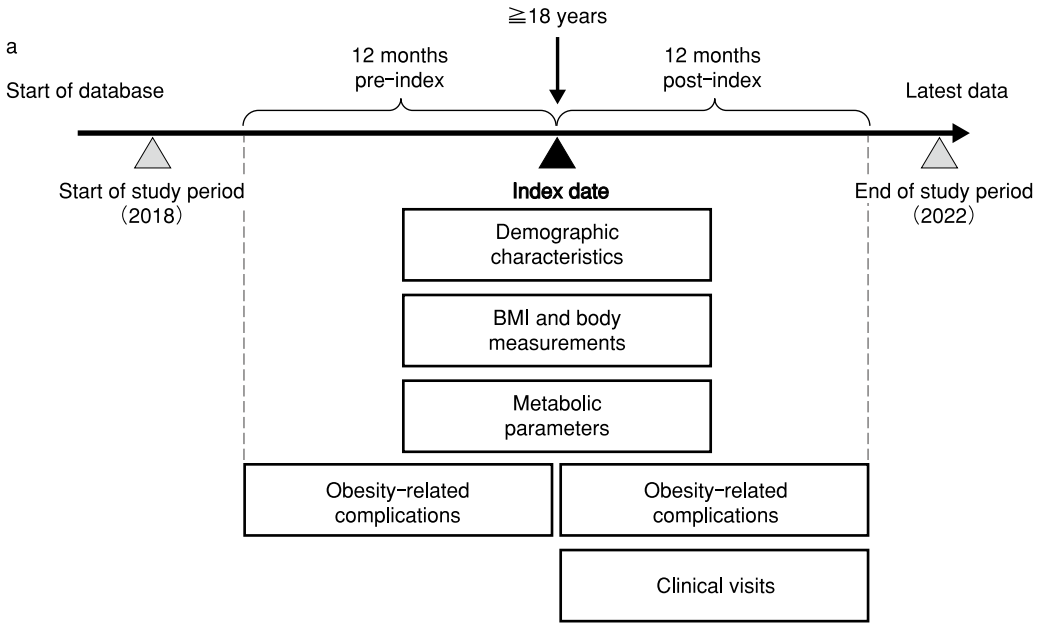

Fig. 1 (a) Study design
BMI: body mass index

nostic codes for glucose intolerance overlaps with T2D and IGT in the multicountry manuscript[24], without access to laboratory values to distinguish IGT from T2D, separate reporting would be methodologically unsound. Therefore, in this analysis, when reporting individual ORC data, we report T2D but not IGT only.

The number of JASSO-defined ORCs (categories: 0, 1, 2, 3, 4, and ≧5 ORCs) recorded at baseline and during follow-up was described for PwOD overall and for each of the BMI categories among PwOD. In addition, the number of JASSO-defined ORCs recorded during follow-up was described for PwHO. The recorded proportions of patients with each specific JASSO-defined ORC were described at baseline and during follow-up for the overall PwOD group and within each of the BMI categories.

3) Clinical visits and hospitalizations

Clinical visits and hospitalizations during the 1-year follow-up period were described for PwHO and PwOD (**Fig. 1a**). Variables included number of visits, number of people hospitalized, number of hospital visits, and hospital visit duration.

4 Statistical analysis

Sample size was determined by the availability of data from patients included in the IQVIA Japan Claims database. Statistical hypothesis testing was not performed and all analyses were descriptive. Missing values were reported as a separate category when possible. Mean, median, and standard deviation are reported for continuous and count variables, and frequency and percentage distributions for categorical variables (including percentage of missing data where applicable). Descriptive statistics are reported separately for PwOD and PwHO within the Obesity Cohort.

Statistical analyses were performed using OMOP analytical tools in Structured Query Language through Snowflake and R (Version 4.2.1;

https://www.r-project.org)[25].

RESULTS

1 Study cohorts

In the IQVIA Japan Claims database, 160,517 individuals met the inclusion criteria for the Obesity Cohort (**Fig. 1b**). After exclusion of patients with ≧1 ORCs from the overall ORC set and no JASSO-defined ORCs within 1 year prior to the index date (N=48,672, 30.3%), there were 68,567 patients (42.7%) in the PwHO group and 43,278 patients (27.0%) in the PwOD group.

2 Baseline demographic and metabolic characteristics

The Obesity Cohort was primarily male (PwHO: *n*=49,713, 72.5%; PwOD: *n*=28,907, 66.8%; **Table 1**). The median age of PwHO was numerically lower than the median age of PwOD (44 years vs. 52 years, respectively). At the index date, BMI was similar in the 2 groups (median 26.0 kg/m^2 and 26.4 kg/m^2 in PwHO and PwOD, respectively).

Most individuals with obesity were in the lowest BMI categories (**Table 1**). Around two-thirds (66.4%) of PwHO and just over half (57.3%) of PwOD were in the ≧25.0 to <27.0 kg/m^2 BMI category. Just over one-fifth (22.0%) of PwHO and around one-quarter (25.4%) of PwOD were in the ≧27.0 to <30.0 kg/m^2 category.

Among PwOD, the percentage of male individuals in each BMI category varied from 61.1% in the ≧35.0 to <40.0 kg/m^2 category to 67.7% in the ≧25.0 to <27.0 kg/m^2 category (**Table 2**). The median age of PwOD in each BMI category decreased as BMI increased, from 52 years in the ≧25.0 to <27.0 kg/m^2 category to 44 years in the ≧40.0 kg/m^2 category.

HbA1c values, lipid levels, and blood pressure values at the index date were similar in the PwHO and PwOD groups (**Table 1**).

3 ORCs

Among PwOD, most people had 1 (*n*=18,887, 43.6%) or 2 (*n*=11,918, 27.5%) JASSO-defined ORCs at baseline, i.e., recorded in the 1-year period before the index date (**Fig. 2**; **Table S2**). The proportion of PwOD with multiple (≧2) JASSO-defined ORCs increased as BMI increased. Specifically, the percentage of participants with exactly 1 JASSO-defined ORC decreased with increasing BMI (from 46.3% of the ≧25.0 to <27.0 kg/m^2 group to 33.9% of the ≧40.0 kg/m^2 group), whereas the proportion with multiple (≧2) ORCs increased progressively across higher BMI categories, indicating an increasing ORC burden with increasing BMI.

During the 1-year follow-up period, around one-quarter of PwOD (*n*=10,447, 24.1%) progressed to having 1 JASSO-defined ORC during follow-up, while the remaining half of PwOD (*n*=21,691, 50.1%) recorded ≧2 JASSO-defined ORCs (**Fig. S1**; **Table S2**). The remainder of PwOD (*n*=11,140, 25.7%) had zero JASSO-defined ORCs recorded. At follow-up, the percentage of PwOD in each BMI category with 1 JASSO-defined ORC declined with increasing BMI, the percentage with 2 ORCs was generally similar across all BMI categories, and the percentage with multiple (≧2) ORCs increased with increasing BMI (**Fig. S1**). ORCs during follow-up were also recorded for PwHO; approximately one-third (34.4%) developed ORCs during this period, with most PwHO experiencing only 1 ORC (*n*=12,852, 18.7%; **Table S2**).

The most commonly recorded JASSO-defined ORCs at baseline among PwOD were hypertension (54.9%), T2D (39.5%), and dyslipidemia (28.2%) (**Fig. 3**). The recorded proportions of hypertension, T2D, OSA, and gout were generally higher for people in the higher BMI categories (**Fig. 4**). Recorded proportions

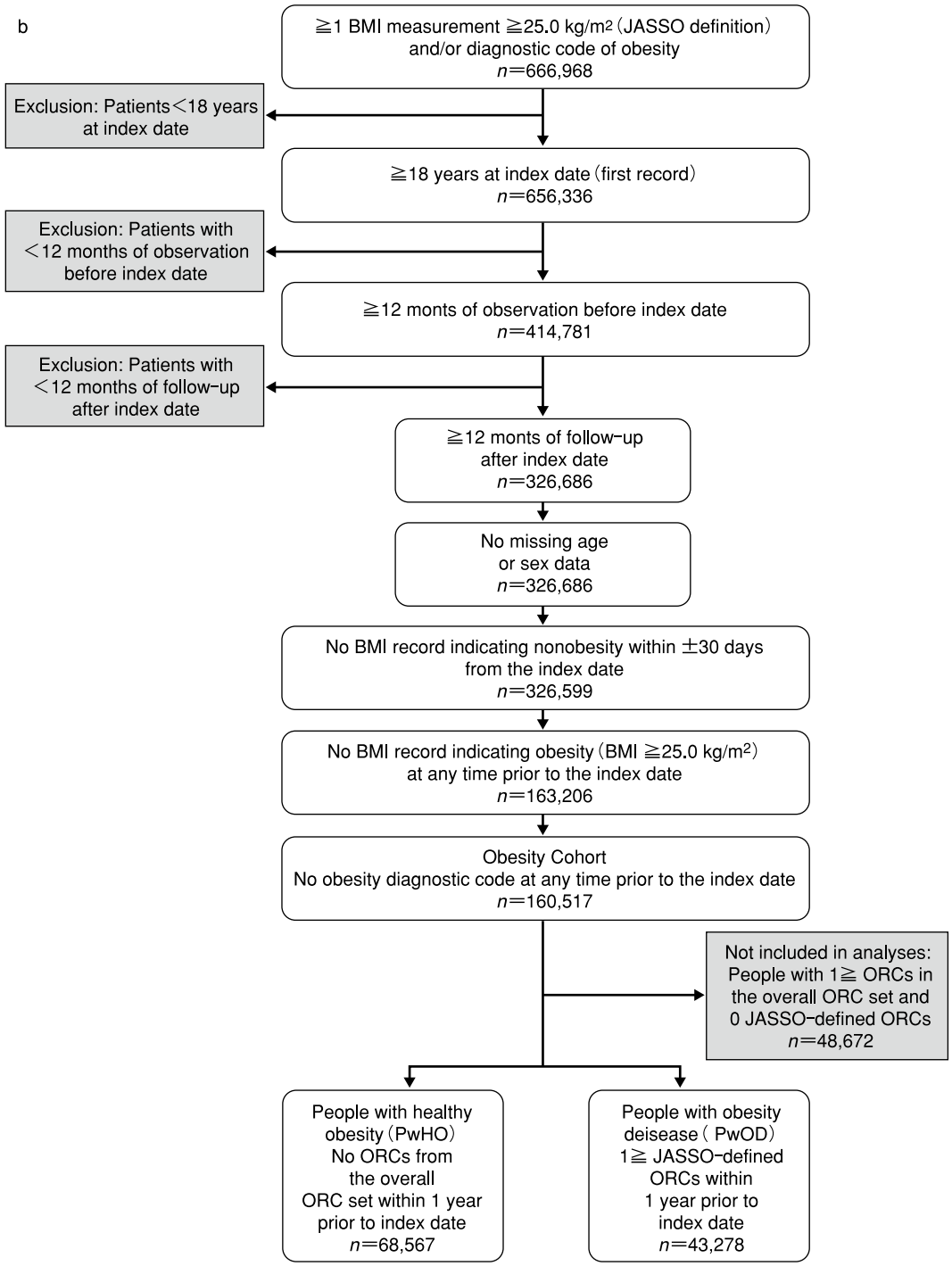

Fig. 1 (b) Patient flow diagram for the Obesity Cohort

BMI: body mass index, JASSO: Japan Society for the Study of Obesity, ORC: obesity-related complication

Table 1　Patient demographic, body measurement, and cardiometabolic characteristics at baseline（Obesity Cohort）

Variable	PwHO (N＝68,567)	PwOD (N＝43,278)
Sex		
Female	18,854（27.5）	14,371（33.2）
Male	49,713（72.5）	28,907（66.8）
Age at index date, years		
Mean（SD）	43.9（10.7）	51.1（11.0）
Median	44.0	52.0
Age category, years		
18–29	7606（11.1）	1489（3.4）
30–39	14,576（21.3）	4595（10.6）
40–49	25,297（36.9）	12,557（29.0）
50–59	16,038（23.4）	13,957（32.2）
60–69	4632（6.8）	8876（20.5）
≧70	418（0.6）	1804（4.2）
Baseline BMI[a], kg/m^2	*n*＝67,650	
Mean（SD）	27.0（2.6）	27.6（3.1）
Median	26.0	26.4
BMI category, kg/m^2	*n*＝67,650	*n*＝43,278
≧25.0 to ＜27.0	44,887（66.4）	24,812（57.3）
≧27.0 to ＜30.0	14,854（22.0）	10,991（25.4）
≧30.0 to ＜35.0	6496（9.6）	5944（13.7）
≧35.0 to ＜40.0	1128（1.7）	1207（2.8）
≧40.0	281（0.4）	324（0.7）
HbA1c[a], %	*n*＝58,468	*n*＝39,549
Mean（SD）	5.6（0.7）	5.9（0.9）
Median	5.5	5.6
HbA1c categories[a], *n*（%）	*n*＝58,468	*n*＝39,549
＜7%	56,719（97.0）	36,039（91.1）
≧7%	1749（3.0）	3510（8.9）
Lipids—triglyceride[a], mg/dL	*n*＝65,160	*n*＝42,676
Mean（SD）	141.1（113.6）	150.0（129.7）
Median	113.0	121.0
Lipids—total cholesterol[a], mg/dL	*n*＝65,133	*n*＝42,657
Mean（SD）	215.5（37.8）	213.8（38.7）
Median	212.6	210.8
Lipids—LDL[a], mg/dL	*n*＝65,146	*n*＝42,674
Mean（SD）	131.4（31.4）	127.4（31.6）
Median	130.0	126.0
Lipids—HDL[a], mg/dL	*n*＝65,150	*n*＝42,672
Mean（SD）	55.9（13.8）	56.4（14.1）
Median	54.0	54.0

Table 1 Patient demographic, body measurement, and cardiometabolic characteristics at baseline (Obesity Cohort) (continued)

Variable	PwHO (N=68,567)	PwOD (N=43,278)
Systolic blood pressure[a], mmHg	*n*=67,099	*n*=43,169
Mean (SD)	126.3 (15.5)	129.6 (17.0)
Median	125.0	128.00
Diastolic blood pressure[a], mmHg	*n*=67,098	*n*=43,168
Mean (SD)	78.3 (11.6)	80.4 (11.8)
Median	78.0	80.0

Data are *n* (%) unless otherwise indicated.
[a]Within ±60 days of the index date (date of first record of BMI ≧25.0 kg/m^2 or diagnostic code of obesity); if there was >1 recorded measurement, the measurement on the date closest to the index date was used.
BMI: body mass index, HbA1c: glycated hemoglobin, HDL: high-density lipoprotein, LDL: low-density lipoprotein, PwHO: people with healthy obesity, PwOD: people with obesity disease, SD: standard deviation

of dyslipidemia, CVD/MI/angina, MASLD/MASH, chronic kidney disease, and disorder of female reproductive system were generally consistent across the BMI categories. The recorded proportion of stroke plus TIA appeared to be lower for people in the higher BMI categories, ranging from 4.4% in the lowest BMI category to 2.1% in the highest BMI category.

During the 1-year follow-up period, the overall recorded proportions of the majority of ORCs among PwOD, including hypertension, T2D, MASLD/MASH, and motor dysfunction, were lower than at baseline (**Fig. S2a**). Relationships between recorded proportions of ORCs and BMI categories during follow-up were generally similar to the patterns at baseline (**Fig. S2b**).

4 Clinical visits and hospitalization

The number of clinical visits was numerically lower for PwHO than PwOD during the 1-year follow-up period (median: 5.0 vs. 19.0 visits) (**Table S3**). The percentage of PwHO hospitalized was numerically lower than the percentage of PwOD hospitalized during follow-up (9.0% vs. 21.6%), and the median hospital visit duration was slightly shorter for PwHO (5.0 days) than for PwOD (6.0 days).

Among PwOD, clinical visits and hospitalizations were similar across the BMI categories. The median number of clinical visits ranged from 19.0 in the ≧25.0 to <27.0 kg/m^2 category to 22.0 in the ≧35.0 to <40.0 kg/m^2 category, the median hospital visit count was either 1.0 or 2.0 visits in all categories, and the median hospital visit duration was either 6.0 or 7.0 days in all categories.

DISCUSSION

In this analysis of the Japanese cohort from the IMPACT-O study, we used data from a commercially available healthcare claims database to describe the sociodemographic and clinical characteristics of adults with obesity in Japan, including PwHO and PwOD. The most common JASSO-defined ORCs among PwOD were hypertension, T2D, and dyslipidemia, and recorded proportions of both hypertension and T2D were higher for people in the higher BMI

Table 2 Patient demographic and body measurement characteristics at baseline across the BMI categories among PwOD (Obesity Cohort)

Variable	PwOD BMI categories[a]				
	≧25.0 to <27.0 kg/m^2 (*n*=21,672)	≧27.0 to <30.0 kg/m^2 (*n*=12,896)	≧30.0 to <35.0 kg/m^2 (*n*=6920)	≧35.0 to <40.0 kg/m^2 (*n*=1407)	≧40.0 kg/m^2 (*n*=383)
Sex					
Female	6998 (32.3)	4206 (32.6)	2489 (36.0)	548 (38.9)	130 (33.9)
Male	14,674 (67.7)	8690 (67.4)	4431 (64.0)	859 (61.1)	253 (66.1)
Age at index date, years					
Mean (SD)	51.7 (10.9)	51.9 (11.2)	49.6 (10.7)	46.2 (10.1)	43.8 (8.9)
Median	52.0	52.0	50.0	46.0	44.0
Age category, years					
18–29	686 (3.2)	421 (3.3)	270 (3.9)	86 (6.1)	26 (6.8)
30–39	2188 (10.1)	1286 (10.0)	806 (11.6)	235 (16.7)	80 (20.9)
40–49	5975 (27.6)	3504 (27.2)	2332 (33.7)	564 (40.1)	182 (47.5)
50–59	7135 (32.9)	4161 (32.3)	2206 (31.9)	377 (26.8)	78 (20.4)
60–69	4816 (22.2)	2833 (22.0)	1084 (15.7)	128 (9.1)	15 (3.9)
≧70	872 (4.0)	691 (5.4)	222 (3.2)	17 (1.2)	2 (0.5)

Data are *n* (%) unless otherwise indicated.

[a]Based on first BMI record.

BMI: body mass index, PwOD: people with obesity disease, SD: standard deviation

categories. The number of clinical and hospital visits was numerically higher for PwOD than PwHO. These results suggest that the burden of obesity may be higher for PwOD than PwHO in Japan, and that disease burden among PwOD increases with increasing BMI. Our results also indicate that some PwHO developed ORCs during the 12-month follow-up.

Many individuals in the present study were PwHO, with no ORCs recorded within 1 year prior to the index date. This result is consistent with the previously noted situation in Japan, in which some people with obesity do not exhibit ORCs[12,26]. As PwHO in our study were generally younger than PwOD (median age 44 vs. 52 years), it is possible that the lack of ORCs among PwHO was associated with their younger age. In fact, ORCs such as hypertension, T2D, and dyslipidemia are known to increase in prevalence with increasing age[27–29]. However, 34.4% of PwHO recorded ≧1 JASSO-defined ORCs during the 1-year follow-up period, indicating that PwHO without current ORCs may represent a transient state rather than a stable, risk-free state.

In both the PwHO and PwOD groups, the majority of patients (around two-thirds) were men. This is consistent with a previous report that the incidence of overweight and obesity (defined as BMI ≧23.0 kg/m^2) among men is approximately double that among women in Japan[30]. We also observed numerically lower median ages as the BMI category increased. A negative relationship between BMI and age in people with BMI 24.0–27.9 kg/m^2 and ≧28.0 kg/m^2 was previously reported, but only for men, in a Chinese epidemiological study[31]. This pattern is also consistent with previously reported trends in Japan, where the prevalence of overweight and obesity has been increasing more rapidly

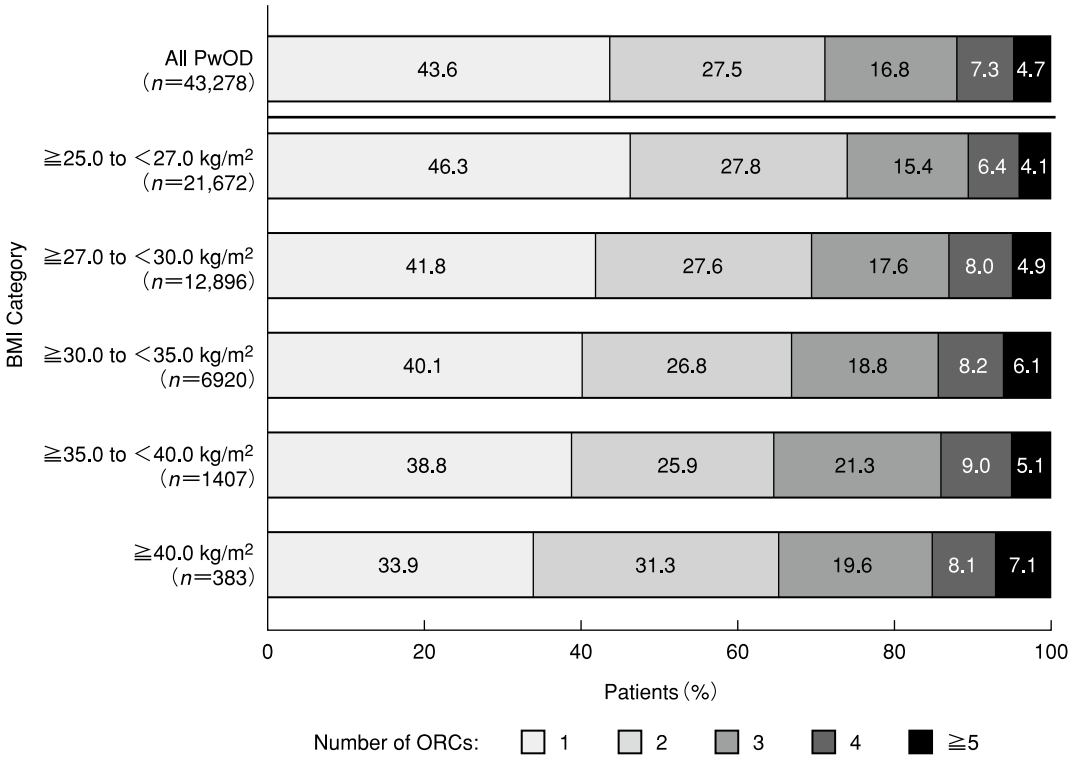

Fig. 2 The number of JASSO-defined ORCs among PwOD and across BMI categories at baseline (Obesity Cohort)

BMI: body mass index, JASSO: Japan Society for the Study of Obesity, ORC: obesity-related complication, PwOD: people with obesity disease

among younger generations, particularly in men[30,32]. The employer-based nature of the IQVIA Japan Claims database, which under-represents older adults, may also have contributed to this observation.

The cardiometabolic characteristics at baseline of PwHO and PwOD were generally similar, likely because those values represent the average characteristics of PwOD with several different ORCs and some PwOD would have been prescribed medication for their ORC(s), resulting in controlled cardiometabolic parameters. The cardiometabolic values at baseline in both PwHO and PwOD were similar to mean values reported for the Japanese population in the 2019 National Health and Nutrition Survey[33], which suggests that the cardiovascular health of PwHO and PwOD was typical for Japanese people. However, 34.4% of PwHO recorded ≧1 JASSO-defined ORCs during the 1-year follow-up period, indicating that some PwHO may have been at an early stage of disease progression or had undetected ORCs at the index date. In truly metabolically healthy PwHO in Japan, the risks of cardiovascular disease and all-cause mortality are not significantly different from metabolically healthy people without obesity[34]. Development of ORCs over time in PwHO may have been related to the presence of visceral obesity, which we could not capture in our study. Further investigation is needed to identify the characteristics of PwHO who may develop ORCs.

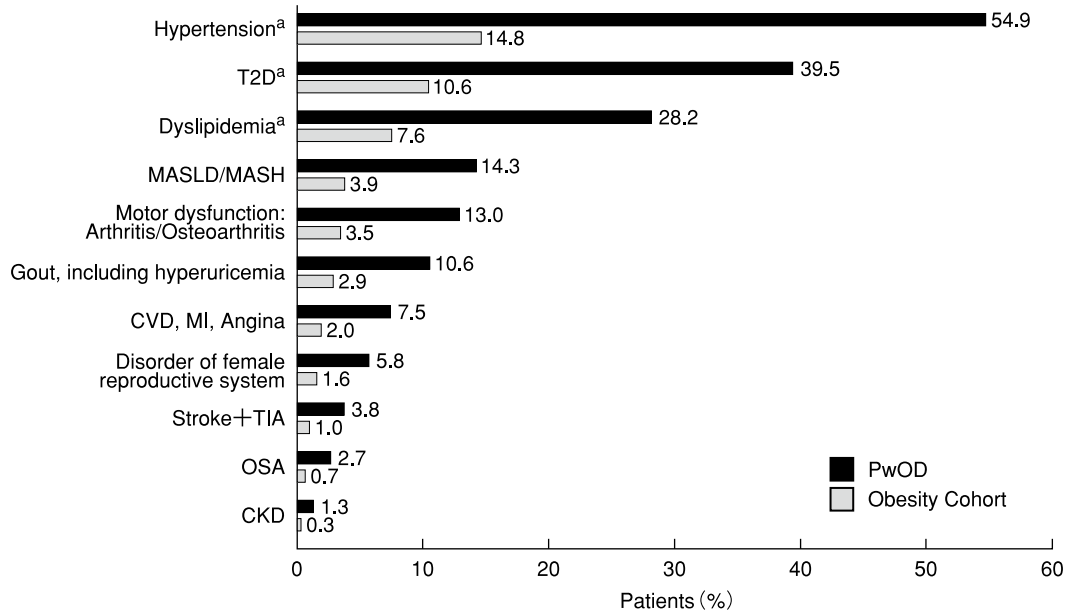

Fig. 3 Recorded proportions of JASSO-defined ORCs at baseline among the whole Obesity Cohort and PwOD group

[a]Diagnosis plus medication.

CKD: chronic kidney disease, CVD: cardiovascular disease, JASSO: Japan Society for the Study of Obesity, MASH: metabolic dysfunction-associated steatohepatitis, MASLD: metabolic dysfunction-associated steatotic liver disease, MI: myocardial infarction, ORC: obesity-related complication, OSA: obstructive sleep apnea, PwOD: people with obesity disease, T2D: type 2 diabetes, TIA: transient ischemic attack

The burden of disease among PwOD was assessed in the present study in 3 ways: the number of JASSO-defined ORCs, recorded proportions of each specific JASSO ORC, and numbers of clinical visits and hospitalizations. Among PwOD at baseline, most patients had between 1 and 3 JASSO-defined ORCs. We also observed differences in the number of JASSO-defined ORCs among PwOD according to their BMI at baseline. The percentage of patients with 2, 3, 4, and ≧5 ORCs at baseline all increased with increasing BMI category. These results are consistent with the result of a pooled analysis of 16 cohort studies from the United States and Europe, in which the risk of developing multiple cardiometabolic comorbidities increased with increasing BMI[35].

Among PwOD, the most common JASSO-defined ORCs were hypertension (54.9%), T2D (39.5%), and dyslipidemia (28.2%), with similar patterns observed in the Prevalent Cohort (**Fig. S3** and **Fig. S4**), supporting the robustness of the result. These findings are consistent with previous studies from the United States and Europe including the original IMPACT-O study, where hypertension and dyslipidemia were the most frequently reported ORCs[24,36-38]. In the present study, the recorded proportions of hypertension and T2D progressively increased as BMI category increased: hypertension increased from 51.1% in the lowest BMI category to 66.6% in the highest, and T2D increased from 36.6% to 51.2%. These BMI-related patterns are similar to those seen in the European

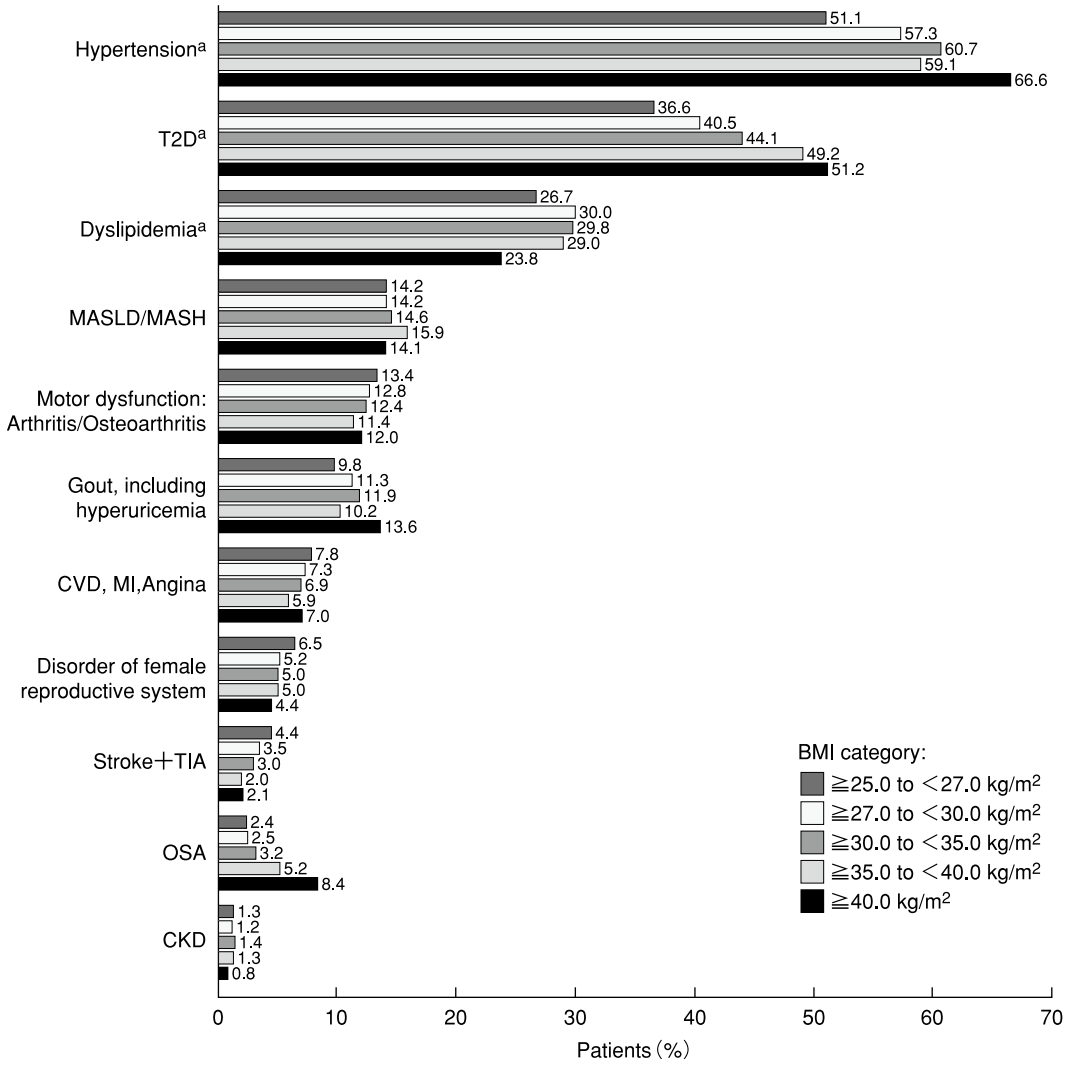

Fig. 4 Recorded proportions of JASSO-defined ORCs at baseline among PwOD, stratified by BMI category (≧25.0 to ＜27.0, ≧27.0 to ＜30.0, ≧30.0 to ＜35.0, ≧35.0 to ＜40.0, and ≧40.0 kg/m^2)

[a]Diagnosis plus medication.

BMI: body mass index, CKD: chronic kidney disease, CVD: cardiovascular disease, JASSO: Japan Society for the Study of Obesity, MASH: metabolic dysfunction-associated steatohepatitis, MASLD: metabolic dysfunction-associated steatotic liver disease, MI: myocardial infarction, ORC: obesity-related complication, OSA: obstructive sleep apnea, PwOD: people with obesity disease, T2D: type 2 diabetes, TIA: transient ischemic attack

RESOURCE study[37] and in a United States population-based study[38]. In contrast, the recorded proportion of patients with dyslipidemia among PwOD did not show a linear increase with increasing BMI, suggesting a heterogenous impact of BMI on different ORCs. This observation is consistent with the J-ORBIT registry study in Japan, which also reported a plateau in dyslipidemia prevalence at higher BMI categories[39]. Dyslipidemia comprises multiple lipid

abnormalities with varying relationships to BMI[40,41]; while high triglyceride levels are strongly associated with obesity, low-density lipoprotein cholesterol levels are more influenced by genetic and dietary factors[40–42]. As the diagnosis code for dyslipidemia in this study captured all lipid abnormalities without distinguishing among subtypes, it was not possible to determine the specific patterns of lipid abnormalities across BMI categories. This may also have contributed to the complex relationship between BMI and dyslipidemia prevalence that was observed in the Obesity Cohort.

Descriptive analysis of the HCRU of PwOD and PwHO in Japan is unique to the IMPACT-O study. PwOD had frequent clinical and hospital visits, with prolonged hospital stays; 21.6% of PwOD required hospitalization. Notably, the median number of clinical visits among PwOD (19.0 visits per year) exceeded the Japanese general population average of 12.1 outpatient visits per capita per year (which itself is among the highest in the Organisation for Economic Co-operation and Development [OECD]), approximately double the OECD average of 6.5 visits. This finding underscores the considerable additional healthcare demand generated by obesity disease beyond the already high baseline utilization rate in Japan. In contrast, PwHO had a median of 5.0 clinical visits per year, which is below the national average, consistent with their younger age and absence of ORCs. The number of clinical visits increased with increasing BMI, although the number of patients with hospitalizations did not, consistent with findings from the European RESOURCE study[37]. This pattern may reflect effective outpatient management of ORCs and the influence of metabolic health status rather than BMI alone on hospitalization risk[43]. The increase in clinical visits with increasing BMI is consistent with the higher percentage of multiple ORCs as BMI increased, suggesting that patients with more ORCs require more frequent medical care. These findings have important implications for healthcare resource planning in Japan, where the healthcare system already faces challenges related to an aging population and high utilization rates.

Strengths of this study included the large sample size of the IQVIA Japan Claims database, the use of JASSO-defined ORCs in the outcome measures to specifically describe PwOD and highlight complications of obesity that are of clinical significance in Japan, and the description of recorded proportions of ORCs and HCRU by BMI category. The study has several limitations inherent to the use of a claims database. As the IQVIA Japan Claims database is designed for patient care rather than research, data may be incomplete (e.g., time since obesity diagnosis was unavailable) and subject to errors such as misclassification or under-recording. This limitation may affect the interpretation of recorded proportions of ORCs. This was a descriptive study without statistical testing between groups and not designed for inferential statistical analysis. Additionally, the overall ORC code set was developed for the multicountry analysis of IMPACT-O[24] and was not validated for Japan, which may result in misestimation of disease burden. The database primarily includes employer-based insurance records, under-representing elderly and unemployed individuals and introducing healthy worker bias[44], possibly underestimating the burden of obesity in Japan. Finally, the inability to capture visceral adiposity data means our PwHO group likely includes individuals at high metabolic risk, which may partially explain the 34.4% of PwHO who developed ORCs during the follow-up period.

CONCLUSION

In conclusion, this analysis of a healthcare claims database in Japan describes that PwOD in Japan experience a burden of disease that often includes multiple ORCs, clinical visits, and hospitalizations. Moreover, the burden of disease in PwOD generally increased with increasing BMI. In addition, around one-third of PwHO developed ORCs during the 1-year follow-up period, suggesting that the absence of ORCs at baseline does not indicate a risk-free state. Taken together, these results suggest that people with obesity in Japan may require early and ongoing medical management and highlight the need for effective interventions to reduce the burden of ORCs.

CONFLICT OF INTEREST

Taisuke Kojima and Mihoko Yoshino are employees of Eli Lilly Japan K.K. and shareholders of Eli Lilly and Company. Taisuke Kojima is a shareholder of Novo Nordisk. Esther Artime is an employee and shareholder of Eli Lilly and Company. Anastasia Lampropoulou is a former employee and former minor shareholder of Eli Lilly and Company. Atif Adam is an employee of IQVIA. Kozo Tanno reports funding from the Research Institute of Strategy for Prevention (RISP) and the Japan Health Insurance Association (Kyokai Kenpo). The RISP receives funding from Eli Lilly Japan K.K.

ETHICS APPROVAL

All analyses performed in this study were in accordance with the data use agreement terms as specified by the data owners. As the data used were deemed commercial assets, there was no requirement for registration of the protocol, nor was there a requirement for ethical review by an Institutional Review Board. Informed consent was not required because the study used de-identified data from the IQVIA Japan Claims database.

FUNDING

This study was funded by Eli Lilly and Company. Eli Lilly and Company was involved in the study design, data collection, data analysis, and preparation of the manuscript.

AUTHOR CONTRIBUTIONS

Esther Artime and Atif Adam were involved in conceptualization of the study. Taisuke Kojima, Anastasia Lampropoulou, and Esther Artime were responsible for funding acquisition, project supervision, and data visualization. Anastasia Lampropoulou and Esther Artime were investigators on the project and responsible for project methodology, administration, and resources. Atif Adam was responsible for methodology, data curation, and formal analysis. All authors were involved in writing the paper and had final approval of the submitted and published versions.

DATA SHARING

The data used for this study were IQVIA proprietary data used under license and, therefore, are not publicly available.

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SUPPLEMENTARY INFORMATION

Part 1: Obesity Cohort

Table S1 List of the overall ORC set defined for the multicountry analysis of IMPACT-O. ORCs were identified using diagnostic codes (ICD-10, SNOMED) and/or medication codes (RxNorm/RxNorm Extension)

Overall ORC set	ORC also included in JASSO-defined set?
Hypertension[a]	Yes[a]
Dyslipidemia[a]	Yes[a]
Heart failure	—
HFpEF	—
ASCVD	Yes[b]
Atrial fibrillation	—
Cerebrovascular disease	—
Stroke	Yes[c]
Coronary artery disease/ischemic heart disease	Yes[b]
Atherosclerosis	—
Peripheral arterial disease	—
T2D[a]	Yes[a]
Impaired glucose tolerance	Yes[d]
Asthma	—
COPD	—
OSA	Yes
Osteoarthritis	Yes[e]
Low back pain	—
Gout, including hyperuricemia	Yes
Motor dysfunction	Yes[e]
MASLD/MASH	Yes
Chronic kidney disease	Yes
Depression[a]	—
Anxiety[a]	—
Dementia	—
Migraine	—
Disorder of female reproductive system	Yes
Breast cancer	—
Esophagus cancer	—
Prostate, endometrial, ovarian, liver cancer	—
Kidney cancer	—
Gastroesophageal disease	—
Urinary incontinence	—

[a]Complications identified by diagnosis codes and/or medication.
[b]In the JASSO-defined ORC set, cardiovascular disease, myocardial infarction, and angina were included in a single ORC category.
[c]Transient ischemic attack was included in the same JASSO-defined ORC category as stroke.
[d]In the JASSO-defined ORC set there were no records of PwOD with impaired glucose tolerance only.
[e]Motor dysfunction in the JASSO-defined ORC set included arthritis and osteoarthritis.
ASCVD: atherosclerotic cardiovascular disease, COPD: chronic obstructive pulmonary disease, HFpEF: heart failure with preserved ejection fraction, ICD-10: International Statistical Classification of Diseases and Related Health Problems 10th Revision, IMPACT-O: epIdeMiology landscape and PAtient Care paThways of Obesity, JASSO: Japan Society for the Study of Obesity, MASH: metabolic-associated steatohepatitis, MASLD: metabolic-associated steatotic liver disease, PwOD: people with obesity disease, ORC: obesity-related complication, OSA: obstructive sleep apnea, SNOMED: Systematized Nomenclature of Medicine Clinical Terms, T2D: type 2 diabetes

Table S2 The number of JASSO-defined ORCs at baseline and during the 1-year follow-up period among PwHO and PwOD (Obesity Cohort)

Number of ORCs	PwHO (N=68,567)		PwOD (N=43,278)	
	ORCs at baseline[a]	ORCs at follow-up[b]	ORCs at baseline[a]	ORCs at follow-up[b]
0	68,567 (100.0)	45,013 (65.6)	0 (0.0)	11,140 (25.7)
1	—	12,852 (18.7)	18,887 (43.6)	10,447 (24.1)
2	—	5573 (8.1)	11,918 (27.5)	9755 (22.5)
3	—	2670 (3.9)	7275 (16.8)	6713 (15.5)
4	—	1250 (1.8)	3164 (7.3)	3029 (7.0)
≧5	—	1209 (1.8)	2034 (4.7)	2194 (5.1)

[a]Diagnosis plus medication codes, within 1 year before assessment date.
[b]Diagnosis plus medication codes, within 1 year after assessment date.
JASSO: Japan Society for the Study of Obesity, ORC: obesity-related complication, PwHO: people with healthy obesity, PwOD: people with obesity disease

Table S3 Clinical visits and hospitalizations during the 1-year follow-up period (Obesity Cohort)

Variable	PwHO (N=68,567)	PwOD (N=43,278)	PwOD BMI categories				
			≧25.0 to <27.0 kg/m^2 (n=21,672)	≧27.0 to <30.0 kg/m^2 (n=12,896)	≧30.0 to <35.0 kg/m^2 (n=6920)	≧35.0 to <40.0 kg/m^2 (n=1407)	≧40.0 kg/m^2 (n=383)
Number of clinical visits							
Mean (SD)	7.8 (9.6)	23.4 (18.2)	22.3 (17.6)	23.9 (18.2)	25.1 (19.4)	25.2 (19.5)	25.4 (19.7)
Median	5.0	19.0	19.0	20.0	21.0	22.0	21.0
Hospitalization							
Number of patients hospitalized, n (%)	6171 (9.0)	9344 (21.6)	4672 (21.6)	2812 (21.8)	1481 (21.4)	297 (21.1)	82 (21.4)
Number of hospitalizations							
Mean (SD)	1.6 (1.5)	2.0 (1.9)	2.0 (1.8)	2.0 (1.8)	2.1 (2.2)	2.1 (1.9)	1.9 (1.6)
Median	1.0	1.0	1.0	1.0	1.0	2.0	1.00
Length of stay[a], days							
Mean (SD)	13.0 (53.1)	15.1 (49.7)	13.6 (28.8)	15.1 (29.3)	16.1 (36.2)	16.2 (36.9)	13.0 (18.9)
Median	5.0	6.0	6.0	7.0	7.0	7.0	6.0

[a]Defined as the total number of days from all hospitalizations during follow-up.
BMI: body mass index, PwHO: people with healthy obesity, PwOD: people with obesity disease, SD: standard deviation

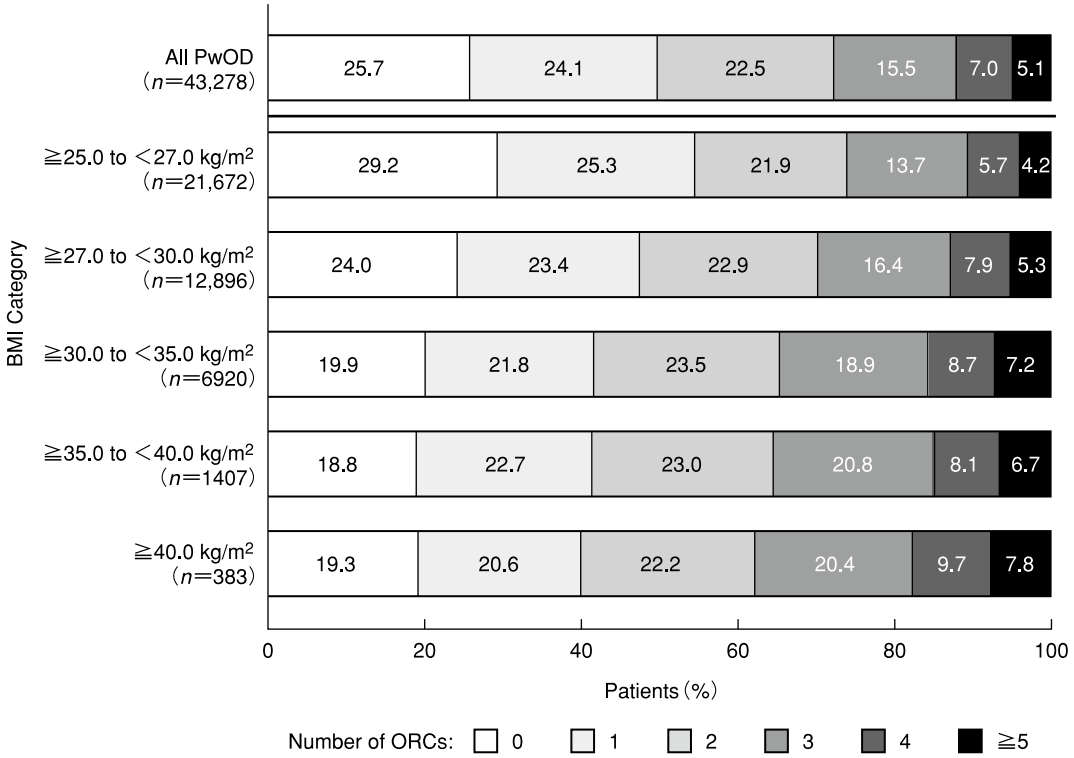

Fig. S1 The number of JASSO-defined ORCs among PwOD and across BMI categories during the 1-year follow-up period (Obesity Cohort)

BMI: body mass index, JASSO: Japan Society for the Study of Obesity, ORC: obesity-related complication, PwOD: people with obesity disease

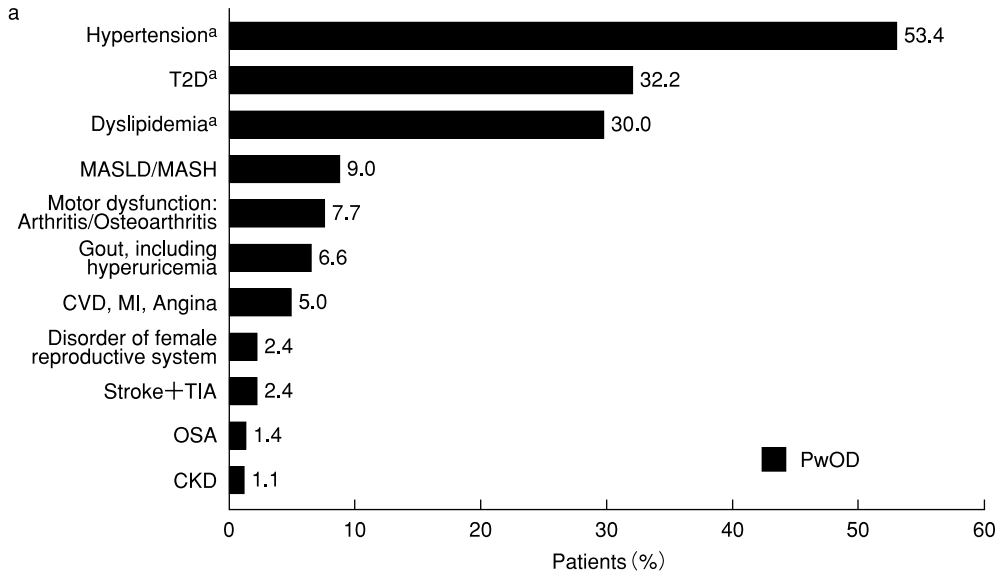

Fig. S2a Recorded proportions of JASSO-defined ORCs during the 1-year follow-up period (Obesity Cohort)

(a) In the overall PwOD population

[a]Diagnosis plus medication.

BMI: body mass index, CKD: chronic kidney disease, CVD: cardiovascular disease, JASSO: Japan Society for the Study of Obesity, MASH: metabolic dysfunction-associated steatohepatitis, MASLD: metabolic dysfunction-associated steatotic liver disease, MI: myocardial infarction, ORC: obesity-related complication, OSA: obstructive sleep apnea, PwOD: people with obesity disease, T2D: type 2 diabetes, TIA: transient ischemic attack

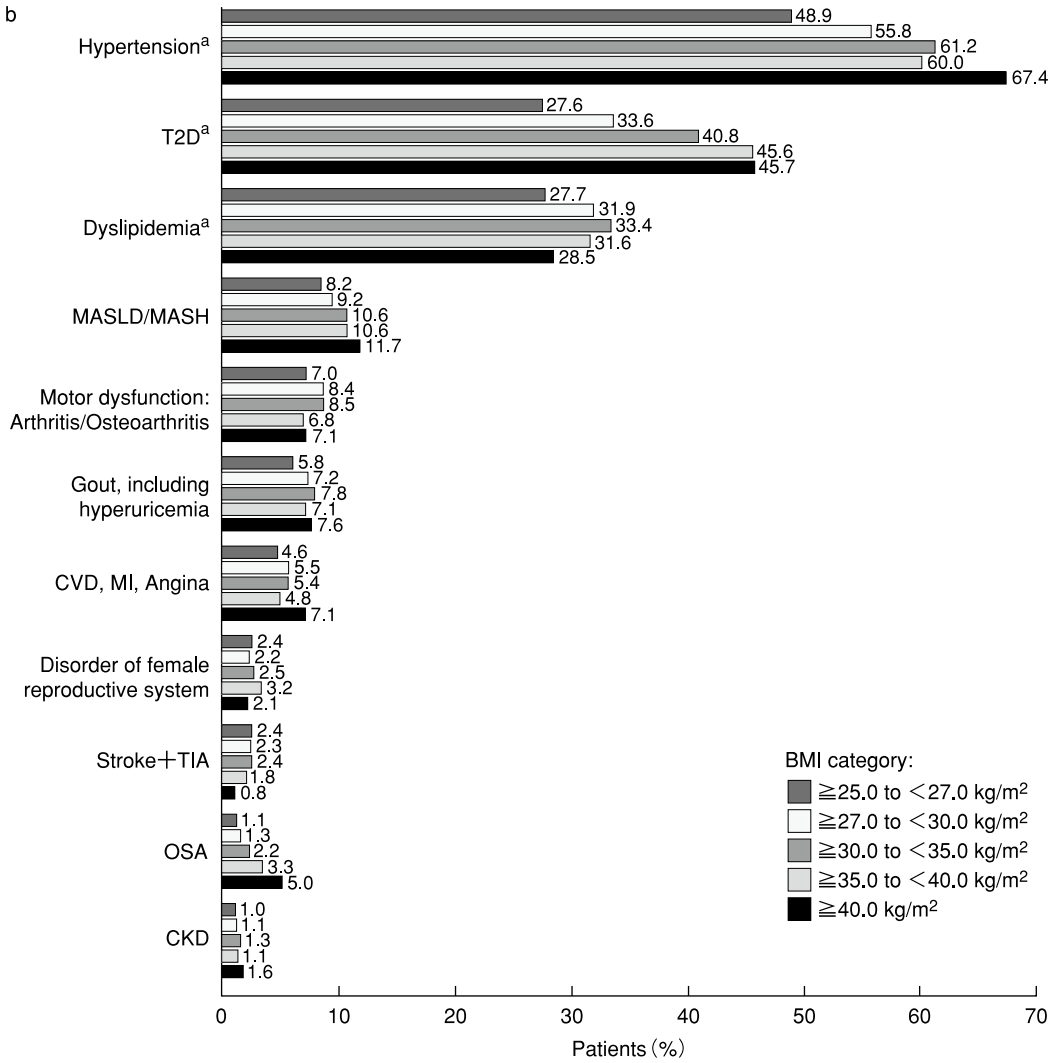

Fig. S2b Recorded proportions of JASSO-defined ORCs during the 1-year follow-up period (Obesity Cohort)
(b) By BMI category

[a]Diagnosis plus medication.

BMI: body mass index, CKD: chronic kidney disease, CVD: cardiovascular disease, JASSO: Japan Society for the Study of Obesity, MASH: metabolic dysfunction-associated steatohepatitis, MASLD: metabolic dysfunction-associated steatotic liver disease, MI: myocardial infarction, ORC: obesity-related complication, OSA: obstructive sleep apnea, PwOD: people with obesity disease, T2D: type 2 diabetes, TIA: transient ischemic attack

Part 2: Prevalent Cohort

Prevalent Cohort Methods

The Prevalent Cohort was used to describe the obesity-related complications (ORCs) of the overall population of adults in Japan with obesity between 2018 and 2022. The Prevalent Cohort consisted of all patients in the IQVIA Japan Claims database within the study period (2018-2022) who were adults (≧18 years at index date), had ≧1 body mass index (BMI) measurement ≧25.0 kg/m^2, with the date of highest BMI record being the index date, with ≧12 months of observation prior to the index date. Exclusion criteria for the Prevalent Cohort were age or sex missing from the patient record.

The disease burden of the whole obesity population in Japan was described using the recorded proportions of each specific Japan Society for the Study of Obesity-defined ORC in the Prevalent Cohort, stratified by BMI category.

Prevalent Cohort Results

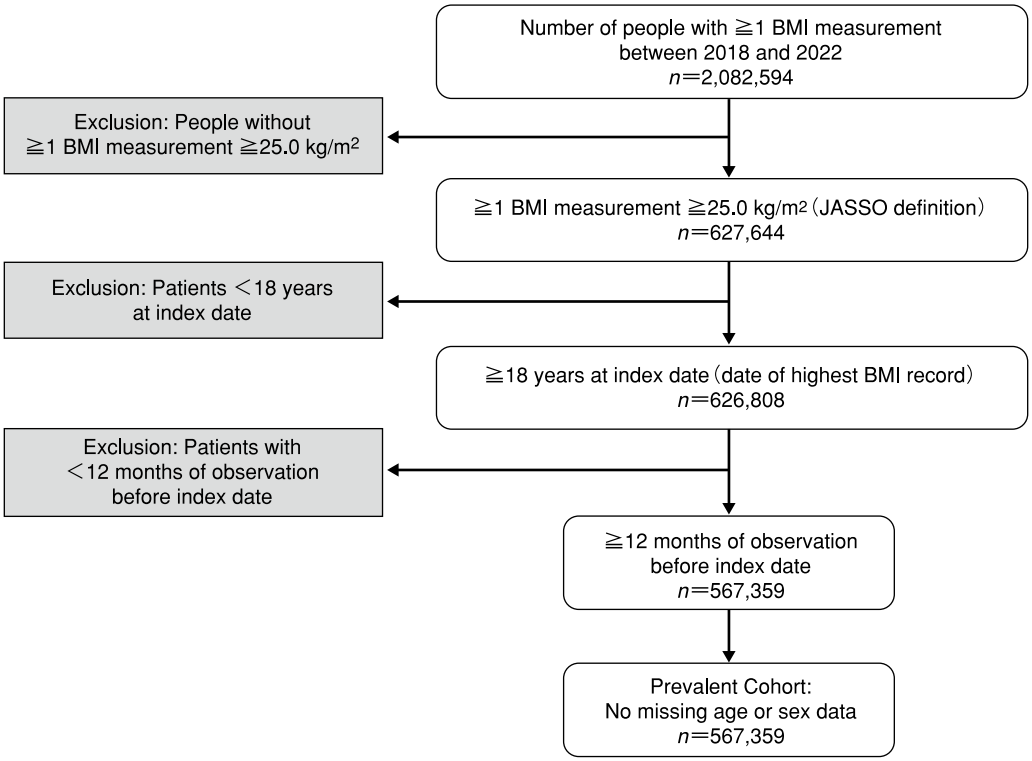

Fig. S3 Patient flow diagram for the Prevalent Cohort
BMI: body mass index, JASSO: Japan Society for the Study of Obesity

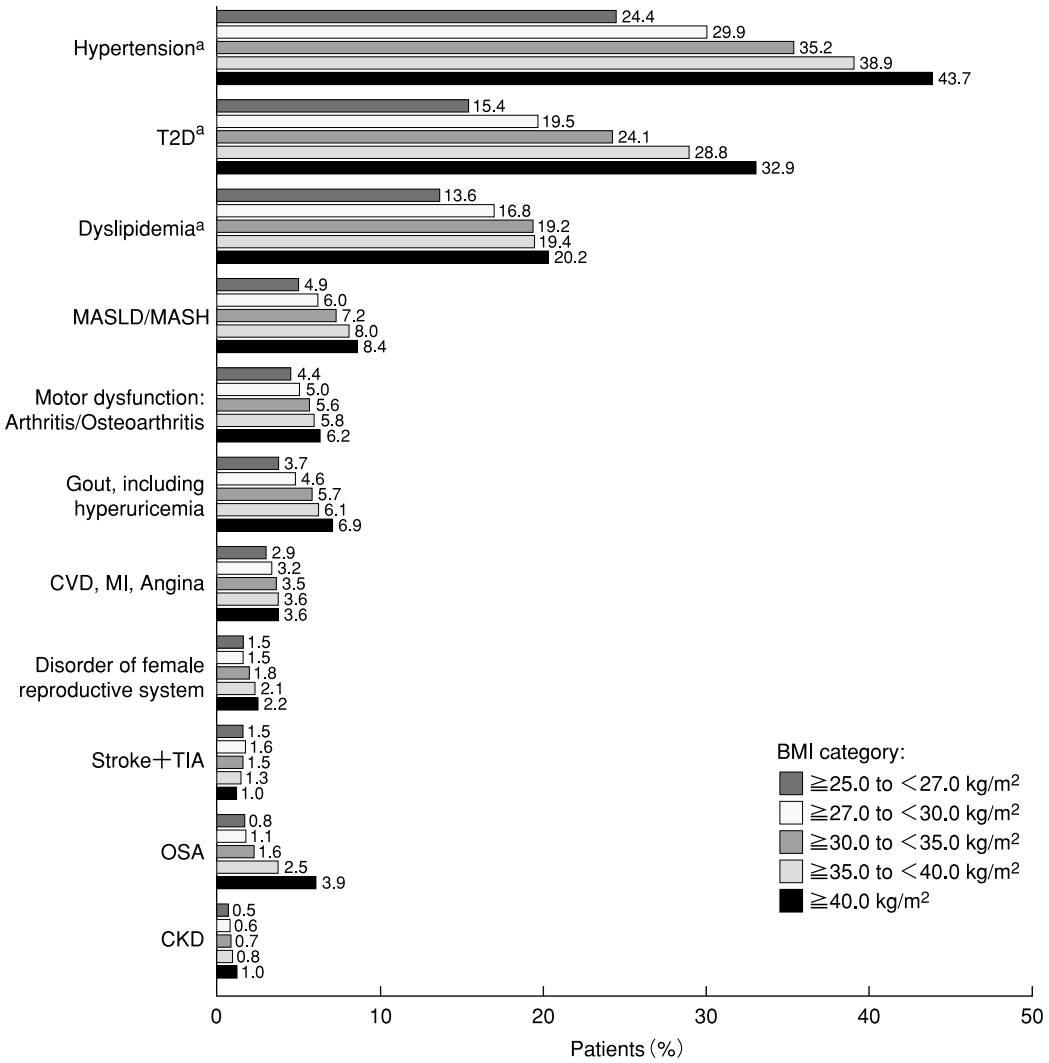

Fig. S4 Recorded proportions of JASSO-defined ORCs by BMI category (≧25.0 to ＜27.0, ≧27.0 to ＜30.0, ≧30.0 to ＜35.0, ≧35.0 to ＜40.0, and ≧40.0 kg/m^2) in the Prevalent Cohort (2018-2022)

[a]Diagnosis plus medication.

BMI: body mass index, CKD: chronic kidney disease, CVD: cardiovascular disease, JASSO: Japan Society for the Study of Obesity, MASH: metabolic dysfunction-associated steatohepatitis, MASLD: metabolic dysfunction-associated steatotic liver disease, MI: myocardial infarction, ORC: obesity-related complication, OSA: obstructive sleep apnea, T2D: type 2 diabetes, TIA: transient ischemic attack