Hospitalization for heart failure in the USA, UK, Taiwan and Japan: an international comparison of administrative health records on 417,385 individual patients.

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Highlights

- Previous reports evaluating international differences in characteristics and survival of patients hospitalized for heart failure (HFH) are mainly from clinical trials and registries with small national samples and biased case-selection.
- This study of nationally representative electronic healthcare records of >400,000 patients with HFH from four countries on three continents reveals marked variations in patient characteristics, healthcare resource utilization and clinical outcomes.
- Better understanding of these international variations may help in the translation of healthcare interventions from one country to another and in the design of international trials.

Abstract

Background: Registries show international variations in the characteristics and outcome of patients with heart failure (HF) but national samples are rarely large, and case-selection may be biased due to enrolment in academic centres. National administrative datasets provide large samples with a low risk of bias. In this study, we compared the characteristics, healthcare resource utilization (HRU) and outcomes of patients with primary HF hospitalizations (HFH) using electronic health records (EHR) from four high-income countries (USA, UK, Taiwan, Japan) on three continents.

Methods and Results: We used EHR to identify unplanned HFH between 2012-2014. We identified 231,512, 10,991, 36,900 and 133,982 patients with a primary HFH from USA, UK, Taiwan and Japan, respectively. HFH per 100,000 population was highest in USA and lowest in Taiwan. Patients in Taiwan and Japan were older but fewer were obese or had chronic kidney disease. LOHS was shortest in USA (median 4 days) and longer in UK, Taiwan and Japan (medians 7, 9 and 17 days, respectively). HRU during hospitalization was highest in Japan and lowest in UK. Crude and direct standardized in-hospital mortality was lowest in USA (direct standardized rates: 1.8 [95%CI:1.7-1.9]%)and progressively higher in Taiwan (direct standardized rates: 3.9 [95%CI:3.8-4.1]%), UK (direct standardized rates: 6.4 [95%CI:6.1-6.7]%) and Japan (direct standardized rates: 6.7 [95%CI:6.6-6.8]%). 30-day all-cause (25.8%) and HF (7.2%) readmissions were highest in USA and lowest in Japan (11.9% and 5.1% respectively).

Conclusion: Marked international variations in patient characteristics, HRU and clinical outcome exist; understanding them might inform health care policy and international trial design.

Key words

Heart failure, outcomes, United States, United Kingdom, Taiwan, Japan

Introduction

Each year, worsening heart failure (HF) is the primary reason for more than 30,000 hospital admissions in Taiwan, 80,000 in the United Kingdom (UK), 200,000 in Japan and one million in the United States of America (USA)[1,4–8] and it will contribute to or complicate many more. There is increasing globalization of clinical research on HF, mostly designed and led by investigators from North America and Europe, but with increasing enrolment from Asian countries. The needs of patients may vary by characteristics such as age and aetiology of disease, whereas outcomes that are often part of the endpoints in trials, such as length of hospital stay (LOHS) and readmissions, may vary according to healthcare system.

Previous reports evaluating international differences in characteristics and outcomes for patients hospitalised with HF (HFH) have been based on those enrolled in clinical trials and registries.[2,13,14,17,22–28] Research is usually conducted by investigators who are specialists working in academic centres; only the patients they care for have the possibility of being enrolled.[26] Patients are often further selected because of protocol inclusion and exclusion criteria. Investigators will often avoid enrolling elderly, frail patients with multiple comorbidities who are less likely to be able to comply with procedures. Many patients who are invited decline to participate and those who do agree are often more educated, more affluent, more optimistic and more adherent to advice, which might explain why they appear to have better outcomes. [29]

Cohorts enrolled by investigators rarely exceed 10,000 patients even when the resources of many are combined; typically most centres will enrol fewer than 30 patients, even if clinical activity is much higher.[30] In contrast, routinely collected administrative data obtained from electronic health records (EHR) provide a comprehensive and unbiased picture of HF-related activity, although perhaps less detailed in some respects, such as clinical presentation and precipitating factors. Thus, clinical trials, registries and administrative data provide complementary information.

Accordingly, we obtained individual patient data from nationally representative EHR from four countries (USA, UK, Japan and Taiwan) on three continents, providing information on patient characteristics, health care resource utilisation (HRU) and short-term clinical outcomes for HFH.

Methods

Data Sources

We obtained EHR from the largest all-payer inpatient care database in the US, a nationally representative sample of the UK population, the national cardiovascular administrative database in Japan and the National Health Insurance Research Database from Taiwan (Table 1). These nations were selected because of the availability of good quality source of nationally representative EHR and administrative health care databases across which we could standardise analyses and for the diversity of health systems, demographics and cultures.

USA- National Readmissions Database (NRD): NRD represents around 50% of all hospitalizations in the US and is the largest national database to examine in-hospital outcomes and readmissions.[34,35] Information on age, sex, race, insurance status, cardiac procedures, LOHS, mortality and cost, readmissions is provided but not post-discharge mortality (Table 1).

England and Wales-Hospital episode statistics / Clinical Practice Research Datalink (HES-CPRD): The CPRD included primary care records for about 5 million (9%) of the UK population in 2012-2014 and is broadly representative in terms of age, sex, and ethnicity.[36,37] Primary care records can be linked to HES, an administrative database which contains information of hospitalizations in England and Wales, including diagnosis and cardiac procedures, for about 60% of patients. CPRD and HES are linked to the Office of National Statistics using each patient's unique National Health Service (NHS) number, which provides place and certified cause of death.

Taiwan- National Health Insurance Research Database (NHIRD): The National Health Insurance program established on March 1, 1995 covers 99.9% of Taiwan's population (about 23 million in 2012). The NHIRD, provided by the Bureau of National Health Insurance of the Department of Health and Welfare, Taiwan, contains outpatient visits, hospitalizations, accident and emergency visits and claims data.[38]

Japanese Registry of All cardiac and vascular Diseases - Diagnosis Procedure Combination [JROAD-DPC]): The JROAD-DPC is an administrative database including nearly all Japanese Circulation Society (JCS)-certified hospitals, including information on patient demographics, in-patient services, prescriptions, cardiac procedures, in-hospital death and data on readmissions but not deaths after discharge. [7,39,40]

Study Population

We included patients aged 18 years or older with a primary HFH from 2012 to 2014 in the UK, Taiwan and Japanese (Figure 1). We included patients with a primary HFH only for 2012 in the USA because follow-up data were not available for 2013-2014. Planned hospitalizations (see methods in supplementary appendix for details) and patients with missing age or sex were excluded from the final analyses (Figure 1). HFH were identified using ICD9 CM codes in the USA and Taiwan and equivalent ICD-10 codes in the UK and Japan (Table 1 and Supplementary Table 7).

Identification of Baseline Characteristics and Co-morbidities

Data on 12 frequently occurring co-morbidities in HF (Coronary artery disease [CAD], atrial fibrillation [AF], diabetes mellitus [DM], hypertension [HTN], chronic lung disease, chronic kidney disease [CKD (codes specific for CKD stage 3 and above)], chronic liver disease, peripheral arterial disease [PAD], obesity, chronic anaemia, pulmonary circulation disorders and alcohol abuse) were extracted using relevant diagnostic codes (Table 1 and Supplementary Table S8).

Codes for each co-morbidity were matched across different healthcare coding systems (i.e., similar ICD-9CM, ICD10 and READ codes for diabetes etc.) to enable comparisons amongst countries (Table 1 and Supplementary Table 8).

Primary and Secondary Outcomes

The main outcomes of interest were differences amongst countries in patient characteristics, in-hospital all-cause mortality and 30-day all-cause readmissions (from the date of discharge) of patients with HFH. Other outcomes of interest were LOHS and HRU during index hospital admission. HRU was based on the proportion of patients receiving coronary angiography, right heart catheterization, mechanical ventilation (invasive and non-invasive), device implantation (permanent pacemakers, implantable cardioverter defibrillator and cardiac resynchronisation therapy), coronary revascularisations (percutaneous and coronary artery bypass grafting), ablations for arrhythmias, cardioversion, and mechanical hemodynamic support during the index hospital stay. Mechanical hemodynamic support was defined by the use of either intra-aortic balloon pump, percutaneous ventricular assisted device or extracorporeal membrane oxygenation in patients not undergoing cardiac surgery. Procedures performed were identified using ICD-9CM procedure codes in the US, Taiwan and Japan, Operating Procedure Code Supplement Fourth Revision (OPCS-4.6) in the UK cohort. (Table 1 and Supplementary Table 9). We also performed extensive standardisation of diagnosis and procedure codes across countries (e.g., matching similar diabetes codes for ICD9 [USA and Taiwan] to ICD 10 [Japan] and READ codes [UK] and coronary angiography codes in ICD9 [USA, Taiwan and Japan] to OPCS4.6 codes [UK]) enabling effective cross country comparisons. Standardisation of codes was performed by two trained cardiologists (V.S and T.N)

Statistical Analysis

Baseline characteristics are presented as medians and quartiles. Four different methods were used to compare in-hospital mortality across countries. 1) Crude in-hospital mortality rates per 100 hospitalizations for HF were calculated for each country. 2) Standardized mortality rates were computed individually for each country based on their standard population distribution for age and sex. 3) Direct standardized mortality rates were also calculated for UK, Taiwan, Japan and US using the standard population distribution of age in the USA in 2010 to provide a single 'universal' standard population accounting for differences in age structures across the countries. 4) Finally, analyses were performed by merging individual patient data from the USA with that from the UK and Japan. Merging data from the USA and Taiwan data was not done due to data-privacy regulations. We performed conventional multivariable logistic regression and inverse probability treatment weighting (IPTW) propensity score analyses to calculate adjusted in-hospital mortality for UK and Japan compared to the USA as the reference population. We adjusted the model for age, sex, relevant co-morbidities including, DM, CKD, AF, CAD, HTN, obesity, chronic lung and liver disease, anaemia, PAD and pulmonary circulation disorders.

To identify patient characteristics that predict high in-hospital mortality or 30-day all-cause readmission, we performed logistic regression analysis and co-morbidity specific adjusted odds ratio (OR) for each country. We adjusted the model for age, sex, CAD, AF, DM, HTN, chronic lung disease, CKD (codes specific for CKD stage 3 and above), chronic liver disease, PAD, obesity, chronic anaemia and pulmonary circulation disorders. Furthermore adjusted odds for in-hospital mortality and 30-day all-cause readmission stratified by age categories (18-34, 35-49, 50-74 and over 75 years) were calculated individually for each country.

In addition to the main analyses, we performed three sensitivity analyses, defined a priori, to assess the robustness of our results. We assumed that patients with an early discharge might have less severe HF. We compared crude, standardized and adjusted in-hospital mortality rates by excluding patients discharged within 24 hours and 48 hours of admission. We also compared in-hospital mortality rates after excluding patients receiving major cardiovascular procedures (defined as percutaneous coronary intervention, coronary artery bypass surgery, implantable cardioverter defibrillator, cardiac resynchronisation therapy and ablations) as it is typical practice in countries like Japan to keep patients in-hospital until all relevant procedures have been performed even if earlier safe discharge would be possible.[2] Finally, we repeated analyses of in-hospital mortality rates after excluding patients admitted at weekends, when there may be less senior supervision of care in some health systems.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

<u>Results</u>

Cohort Baseline Characteristics

From more than one million HFH, we identified 231,512, 10,991, 36,000 and 133,982 unique patients who had an unplanned primary HFH in the USA, UK, Taiwan and Japan, respectively. In Taiwan and Japan, patients aged >85 years comprised a much greater proportion of HFH compared to the UK and US (Table 2 and Figure 2). The highest prevalence of CAD, DM and HTN was in Taiwan (CAD 73%, DM 56.3%, HTN 90%) and lowest in Japan (CAD 34.2%, DM 23.6%, HTN 56.2%). Taiwanese patients also had the highest rates of comorbid liver and lung disease. In contrast, the prevalence of obesity (USA 18.0%, UK 10.8%, Taiwan 1.4%, Japan 0.1%) and CKD

(US 40.1%, UK 33.9%, Taiwan 19.2%, Japan 12.4%) was higher in the USA and UK. More patients in the UK (23.6%) and the USA (26.7%) were discharged within 24 hours of admission compared to Japan (5.5%) and Taiwan (2.1%).

Inpatient Healthcare Resource Utilisation

The proportion of patients with HFH receiving diagnostic procedures including coronary angiography and right heart catheterization during hospitalisation were highest in Japan (coronary angiogram 20.7%; right heart catheterization 11.9%) and lowest in the UK (coronary angiogram 4.3%; right heart catheterization 0.2%). Similar trends were observed in the use of mechanical ventilation (invasive and non-invasive), mechanical hemodynamic support and cardioversions suggestive of worse HF severity in Japan. The utilisation of other common cardiovascular procedures including coronary revascularisation, device implantation and ablations during index hospitalisation are outlined in Table 3.

Length of hospital stay, in-hospital mortality and 30-day readmission (readmission due to any cause and due to HF)

The USA had the shortest stay [median LOHS; 4 days, (25th to 75th percentile 2-6)] compared to the UK [median LOHS; 7 days (3-15)], Taiwan [median LOHS; 9 days (4-10)], and Japan [median LOHS; 17 days (10-28)] (Table 4). The crude in-hospital all-cause mortality rate (per 100 hospitalizations for HF) and direct age standardized in-hospital mortality rate (standardized for US age distribution in 2010) for each country are illustrated in Table 4.

The crude and standardized rates for in-hospital mortality among patients with HFH were highest in Japan (direct standardized rates 6.7 per 100 hospitalizations for HF, 95%CI 6.6-6.8), followed by UK (direct standardized rates 6.4 hospitalizations for HF, 95%CI 6.1-6.7), Taiwan (direct standardized rates 3.9 hospitalizations for HF, 95%CI 3.8-4.1) and the USA (direct standardized rates 1.8 per 100 hospitalizations for HF, 95%CI 1.7-1.9). Furthermore, the adjusted odds for in-hospital mortality was higher in the UK, compared to Japan and the US (reference-US patients with HFH) (Figure 3 A-B). The proportion of patients readmitted in 30-days due to any cause and due to HF were similar in the UK, USA, and Taiwan (22-25%) but much lower in Japan (12%), inverse associated with the index LOHS. The adjusted odds for 30-day readmission were similar in the UK and USA, but much lower in Japan. (Figure 3 C-D)

Factors predicting in-hospital mortality and 30-day readmissions in each country

Factors predicting in-hospital mortality and 30-day readmission due to any cause were generally similar across the countries (Figures 4 and 5). In multivariable logistic regression analyses, clinical characteristics including age > 65 years and CKD were associated with in-hospital mortality in all four countries. However, DM, obesity and CAD were all associated with a lower in-hospital mortality in all countries (Figure 4). CKD and chronic lung disease predicted a higher risk of 30-day readmission, but obesity was associated with a lower rate of readmissions in all four countries. In multivariable analyses stratified by age, adjusted odds for in-hospital death increased with age in all countries but 30-day all-cause readmission were lower in older age groups (age > 75 years) in all countries (odds ratios: UK:0.45, 95% CI 0.27-0.76, USA: 0.76, 95% CI 0.71-0.85, Japan:0.77, 95% CI 0.71-0.85) except Taiwan (1.25, 95% CI 0.94-0.1.68) (Supplementary Table 1).

Sensitivity analyses

Sensitivity analyses were performed for each country by excluding patients discharged within 24 and 48 hours, those patients who underwent major cardiovascular procedures during hospitalisation and those patients admitted in the weekends, all of which yielded results similar to the original analyses (Supplementary Tables 2-5).

The short-term outcomes of HFH for all four countries are summarised in the central illustration

Discussion

To our knowledge this is the first attempt to compare patients with a HFH using nationally-held EHR across continents and cultures, providing important insights into differences in patient characteristics, HRU and short-term clinical outcomes. We found marked differences in age, rates of obesity and CKD, in-hospital mortality, LOHS, HRU and 30-day readmissions. However, predictors for in-hospital mortality and 30-day readmission were consistent.

Rates of Hospitalisation for Heart Failure

The national rates for HFH per 100,000 people varied widely (Supplementary Table 6), being much higher in the USA compared to other countries (despite a lower estimated prevalence of HF than Taiwan and a similar prevalence to the UK)[4,37,54–56], suggesting a lower threshold for HFH in the USA (Supplementary Table 6).[53] Differences in the rates for HFH may reflect differences in health care financing and delivery, medical litigation, earlier identification of HF decompensation, or lower thresholds for hospital admission.[57]

Heterogeneities in baseline characteristics

The mean age of Asian patients in our study was more than a decade older than Asian HFH patients in the ADHERE-Asia Pacific and REPORT-HF registries, and Asian HF patients enrolled in the PARADIGM-HF and ATMOSPHERE trials.[16,23,28] This suggests that clinical registries and trials selectively enrol younger patients. Enrolling younger patients might be appropriate for a therapeutic clinical trial, where the purpose is to improve wellbeing or outcome because they might be more likely to respond to therapy. However, caution is required in extrapolating the trial findings to older populations where the disease and outcome may be less modifiable. On the other hand, clinical registries often aim to be epidemiologically representative and to reflect clinical practice, which should not exclude elderly patients.

A much higher proportion of patients with a HFH in Japan and Taiwan were aged >75 years (85.4% in Japan compared to 51.2% in the USA). There are several potential explanations for this. Life expectancy for the general population is longer in Japan than in Taiwan, UK or USA and that may be reflected in the demographics of patients with a HFH.[41,42] Obesity is a risk factor for HF, especially HF with preserved ejection fraction (HFpEF), which may provoke the earlier onset of HF.[43–45] The threshold to admit elderly patients may differ across countries due to differences in the infrastructure for care in the community.[41,46]

Our study confirms previous reports of a high prevalence of DM despite a near absence of overt obesity in Asian HF patients.[18,47] Patients from Taiwan not only had the highest prevalence of traditional risk factors for HF (HTN, DM, CAD) but the highest prevalence of several non-cardiac co-morbidities including chronic lung (due to high rates of smoking) [48,49] and liver disease (reflecting a high prevalence of hepatitis B and hepatitis C). [50,51]

Difference in healthcare resource utilisation

Despite the lowest prevalence of CAD, almost 20% of patients with HFH in the Japan had an in-patient coronary angiogram. Although ischemic heart disease is the most common cause for HF in the West, only a small fraction of HFH in the US (7.3%) and the UK (4.3%) were associated with coronary angiograms, consistent with a prior report from the US demonstrating low rates of investigation for ischemia in new onset HF.[52] Hemodynamic assessment using pulmonary artery catheters was also high in Japan (12%) compared to the USA (4.0%), UK (0.2%) and Taiwan (1.7%). In-patient procedural HRU was lowest in the UK, in keeping with the substantially lower expenditure on healthcare in the UK {reference}.[53] There are many factors that could have driven the geographic differences in HRU including per capita health care expenditure, reimbursement mechanisms, differences in patient characteristics, severity of HF at the time of admission along with varying cultural and practice patterns, including potentially greater reliance on non-invasive imaging assessment (cardiac computed tomography, stress echocardiograms, nuclear imaging, magnetic resonance imaging etc., which were not captured in these records) in the USA and UK. These differences in HRU require further investigation to determine whether higher expenditure improves outcome meaningfully.

Differences in clinical outcomes

Clinical trials and registries of HF, where patients are enrolled across multiple regions, should be cognizant of very differing LOHS, in-hospital mortality and LOHS.[13] The US had the lowest crude and direct standardized in-hospital mortality rates, whereas Japan and the UK were among the highest, with Taiwan in the middle. Whether this represents the younger population of obese HF patients being admitted in the US, differences in threshold for hospitalisation, variations in practice patterns, procedural utilisation or approach to out of hospital care (nursing facility, home care and end of life care) is unclear. LOHS might explain some of the variation in in-patient mortality. Ideally, mortality should be measured over a fixed period (for instance 30 days). Daily mortality in the first 2-3 days after a HFH may exceed 1% but declines rapidly thereafter to a plateau closer to 0.1% and is probably similar whether the patient remains in hospital or is discharged. Extending LOHS from 5 days to 30 days (ie: by 25 days) might increase in-hospital mortality by 2.5% without any difference in 30-day mortality. Our sensitivity analyses performed by excluding patients discharged within 24 or 48 hours (patients who were likely to have less severe HF) were similar to the main analyses. The higher in-hospital mortality rates observed in the UK may reflect a higher threshold for admission and consequently a population with more severe HF. [57]

Our results highlight the complex relationship between inpatient HRU and in-hospital mortality, with both the UK and Japan having higher in-hospital mortality rates, despite the sharp disparities in HRU (highest HRU in Japan and lowest in the UK). Finally, differences in mortality could be partially explained by the differences in the provision of out of hospital care, including community HF services and end of life care which is crucial in patients with advanced HF. In the USA, a substantial proportion of patients with severe chronic illness die at home or in hospices;[58] whereas end of life care in UK and Japan is predominantly hospital centric.[59] The availability of out of hospital services and the shorter LOHS in the USA could be explained by patient preference, higher daily hospital costs, and the economic pressure to find alternatives to hospitalisation (hospice, home care services and palliative care). [60–62]

Uniqueness and Strengths of the data and analysis

Extensive standardisation of diagnostic and procedure codes across countries was done independently by two cardiologists, enabling cross-country comparisons. To the authors' knowledge, this analysis is the first to compare several large, nationally-representative EHR and administrative databases, whilst utilizing standardized coding algorithms.[33] We acknowledge that there will be some misclassification in EHR and administrative health care databases, we believe that the large sample in all four countries renders our results valid.

Limitations

Our analysis has some important limitations. Several diagnostic and prognostic variables, including biomarkers, echocardiograms, and blood pressure were not available, precluding identification of HF phenotype and the application of existing mortality prediction models derived from registries and trials. We were not able to differentiate de novo HF admissions from acute decompensations of chronic HF; the first hospitalisation in this analysis is the first for the study period and not necessarily the first ever HFH. However, this should not impact the population level estimates of the HFH burden across countries. We did not have information of the out of hospital mortality in the US and Japan; readmissions may be reduced both by good care or by a high mortality. Another limitation of research in any setting but perhaps more often with EHR is the potential for misclassification of some diseases or events. Ultimately, we are limited by the methods by which diagnoses and events are recorded. Wherever possible, definitions and algorithms that have been validated in these data sources were used to identify both the diseases of interest as well as complications. Despite performing extensive coding conversions across all countries, coding patterns could have still been influenced by differences in health care reimbursements.

Conclusions:

An analysis of EHR on more than one million HFH from the USA, UK, Taiwan and Japan showed marked differences in age, rates of obesity and CKD, in-hospital mortality, LOHS, HRU and 30-day readmissions. However, predictors for in-hospital mortality and 30-day readmission were fairly consistent. Our findings might provide insights for physicians and healthcare providers to improve care for patients with HF globally. Furthermore, as HF clinical trials become more global, greater understanding of regional factors that influence outcomes may be important for their design, interpretation and implementation.

Acknowledgement/Contributors

VS, TN, JKQ, JS and JGFC conceived and designed the analysis. Standardisation and individual matching of diagnoses (cardiac and non-cardiac co-morbidities) and procedure codes (healthcare resource utilisation) across the four countries was performed by VS and TN. VS, TN, TFC, and MN did the statistical analysis. All authors contributed to analysing the data, interpreting the results, drafting the manuscript and the revisions.

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Table 1 Data Source, Diagnosis and Procedural Coding Systems in 4 Countries

Country	Data Source	Generalizability	HF diagnosis	Coding system for co-morbidities	Coding system for procedures during index hospitalization
United States	NRD	50% of all hospitalizations	Hospitalization with a primary ICD-9-CM diagnosis code for HF	ICD-9-CM: co-morbidities recorded at the time of admission	ICD-9-CM procedural codes
United Kingdom (England and Wales only)	HES linked to CPRD and ONS	7% of the population	Hospitalization with a primary ICD-10 diagnosis code for HF	READ codes: co-morbidities recorded at outpatient encounter prior to the admission	OPCS 4.6 procedural codes
Taiwan	NHIRD	99% of the entire population	Hospitalization with a primary ICD-9-CM diagnosis code for HF	ICD-9-CM: co-morbidities recorded at outpatient encounter prior to the admission	ICD-9-CM procedural codes
Japan	JROAD-DPC	~ 600 health-care providers	Hospitalization with a primary ICD-10 diagnosis code for HF	ICD-10: co-morbidities recorded at the time of admission	ICD-9-CM procedural codes

HF = heart failure; NRD = National Readmission Database; HES = Hospital Episode Statistics; CPRD = Clinical Practice Research Datalink; ONS = Office of National Statistics; NHIRD = National Health Insurance Research Database; JROAD-DPC = Japanese Registry Of All cardiac and vascular Diseases-Diagnosis Procedure Combination; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10 = International Classification of Diseases, Tenth Revision.

Table 2 Baseline Characteristics of Patients with HF Hospitalization				
Variable	NRD United States (n = 231,512)	HES-CPRD United Kingdom (n = 10,991)	NHIRD Taiwan (n = 36,900)	JROAD-DPC Japan (n = 133,982)
Mean age in years	73.1±14.1	78.8±12.9	74	78.7±12.5
Age, n (%)				
18-35	2,802 (1.2)	71 (0.7)	59 (0.2)	143 (0.1)
36-45	7,083 (3.1)	146 (1.3)	367 (1.0)	650 (0.5)
46-55	20,002 (8.6)	454 (4.1)	1,077 (2.9)	2,212 (1.7)
56-65	35,431 (15.3)	870 (7.9)	2,542 (6.9)	4,444 (3.3)
66-75	47,678 (20.6)	1,856 (16.9)	5,122 (13.6)	12,092 (9.0)
76-85	64,756 (28.0)	3,812 (34.6)	7,120 (19.3)	22,613 (16.9)
>85	53, 760 (23.2)	3,791 (34.5)	20,613 (55.9)	91,828 (68.5)
Women, n (%)	116,066 (50.1)	5,665 (48.5)	18,735 (50.8)	66,424 (49.6)
Co-morbidities, n (%)				
Coronary artery disease	127,533 (53.2)	4,329 (39.4)	27,773 (75.3)	45,802 (34.2)
Atrial fibrillation	97,173 (40.6)	3,640 (33.1)	13,652 (37.0)	40,472 (30.2)
Diabetes mellitus	102,409 (44.1)	3,076 (28.0)	20,785 (56.3)	31,627 (23.6)
Hypertension	177,840 (76.8)	6,827 (62.1)	33,214 (90.0)	75,234 (56.2)
Chronic lung disease	83,743 (36.2)	2,691 (24.5)	23,161 (62.8)	10,809 (8.1)
Chronic kidney disease	92,797 (40.1)	3,731 (33.9)	7,201 (19.2)	16,581 (12.4)
Chronic liver disease	6,881 (3.0)	133 (1.2)	12,310 (33.4)	3,949 (3.0)
Peripheral arterial disease	28,127 (12.2)	1,440 (13.1)	7,041 (19.1)	7,093 (5.3)
Obesity	41,589 (18.0)	1,186 (10.8)	524 (1.4)	148 (0.1)
Chronic anemia	69,853 (30.2)	1,352 (12.3)	12,815 (34.7)	14,220 (10.6)
Pulmonary circulation disorders	878 (0.4)	131 (1.2)	2,258 (6.1)	1,850 (1.4)
Alcohol abuse	7,229 (3.1)	218 (2.0)	535 (1.4)	82 (0.1)
Discharged within 24 hours of admission, n (%)	22,764 (9.5)	1,872 (17.0)	421 (1.4)	5,428 (4.1)
Discharged within 48 hours of admission, n (%)	63,969 (26.7)	2,591 (23.6)	783 (2.1)	7,351 (5.5)

Abbreviations as in **Table 1**. Values are n (%) or mean ± SD, unless otherwise indicated.

Table 3 Health Care Resource Utilization during Hospital Stay

Variable	NRD United States (n = 231,512)	HES-CPRD United Kingdom (n = 10,991)	NHIRD Taiwan (n = 36,900)	JROAD-DPC Japan (n = 133,982)
In-hospital procedures, n (%)				
Coronary angiogram	17,583 (7.3)	474 (4.3)	3818 (10.3)	27,785 (20.7)
Right heart catheterization	9634 (4.0)	16 (0.2)	637 (1.7)	15,877 (11.9)
Mechanical ventilation	20,852 (9.0)	594 (5.4)	2772 (7.5)	24,852 (18.6)
Device implantation	5374 (2.2)	308 (2.8)	319 (0.9)	3,300 (2.5)
Revascularization	2941 (1.2)	63 (0.6)	1232 (3.3)	7,284 (5.4)
PCI	2211 (1.0)	51 (0.5)	1114 (3.0)	6,517 (4.9)
CABG	730 (0.3)	12 (0.1)	118 (0.3)	767 (0.6)
Ablations / Cardioversion	2869 (1.2)	52 (0.53)	121 (0.3)	4,396 (3.3)
Cardioversion	2342 (1.0)	49 (0.5)	101 (0.3)	3,729 (2.8)
Ablations for atrial or ventricular arrhythmias	525 (0.2)	3 (0.03)	20 (0.1)	667 (0.5)
Mechanical hemodynamic support	1137 (0.4)	23 (0.2)	164 (0.4)	2,828 (2.1)

PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; other abbreviations as in **Table 1**. Device implantation incudes permanent pacemakers, implantable cardioverter defibrillator and cardiac resynchronization therapy. Mechanical hemodynamic support includes intra-aortic balloon pump, percutaneous ventricular assisted device, extracorporeal membrane oxygenation in patients not undergoing CABG or valvular surgery.

Table 4 Clinical Outcomes

Variable	NRD United States (n = 231,512)	HES-CPRD United Kingdom (n = 10,991)	NHIRD Taiwan (n = 36,900)	JROAD-DPC Japan (n = 133,982)
Median length of hospital stay, days	4 (2 - 6)	7 (3 - 15)	9 (4 - 10)	17 (10 - 28)
Crude in-hospital mortality, n (rate per 100 hospitalizations for HF)	7,264 (3.2)	1,350 (12.2)	2,243 (6.1)	15,823 (11.8)
*Age standardized in-hospital mortality, rate per 100 hospitalizations for HF(95% CI)	1.8 (1.7-1.9)	6.7 (6.6-7.1)	3.8 (3.6-3.9)	7.0 (6.9-7.2)
Direct age standardization using United States age distribution for 2010 in-hospital mortality, rate per 100 hospitalizations for HF (95% CI),	1.8 (1.7-1.9)	6.4 (6.1-6.7)	3.9 (3.8-4.1)	6.7 (6.6-6.8)
30-day all-cause readmission, n (%)	57,880 (25.8)	2,237 (25.1)	8,100 (22.0)	14,055 (11.9)
30-day HF readmission, n (%)	16,147 (7.2)	486 (5.5)	2,058 (5.6)	5,977 (5.1)

Values are n (%) or median (interquartile range), unless otherwise indicated. CI = confidence interval; other abbreviations as in **Table 1**. *Age standardized rates are based on 2010 population in United States and Japan, and 2013 European standardized population in the United Kingdom; Direct standardization for all countries was performed using US age distribution of 2010

Figure 1. Flow Diagram for Identifying Study Population in the USA, UK, Taiwan and Japan

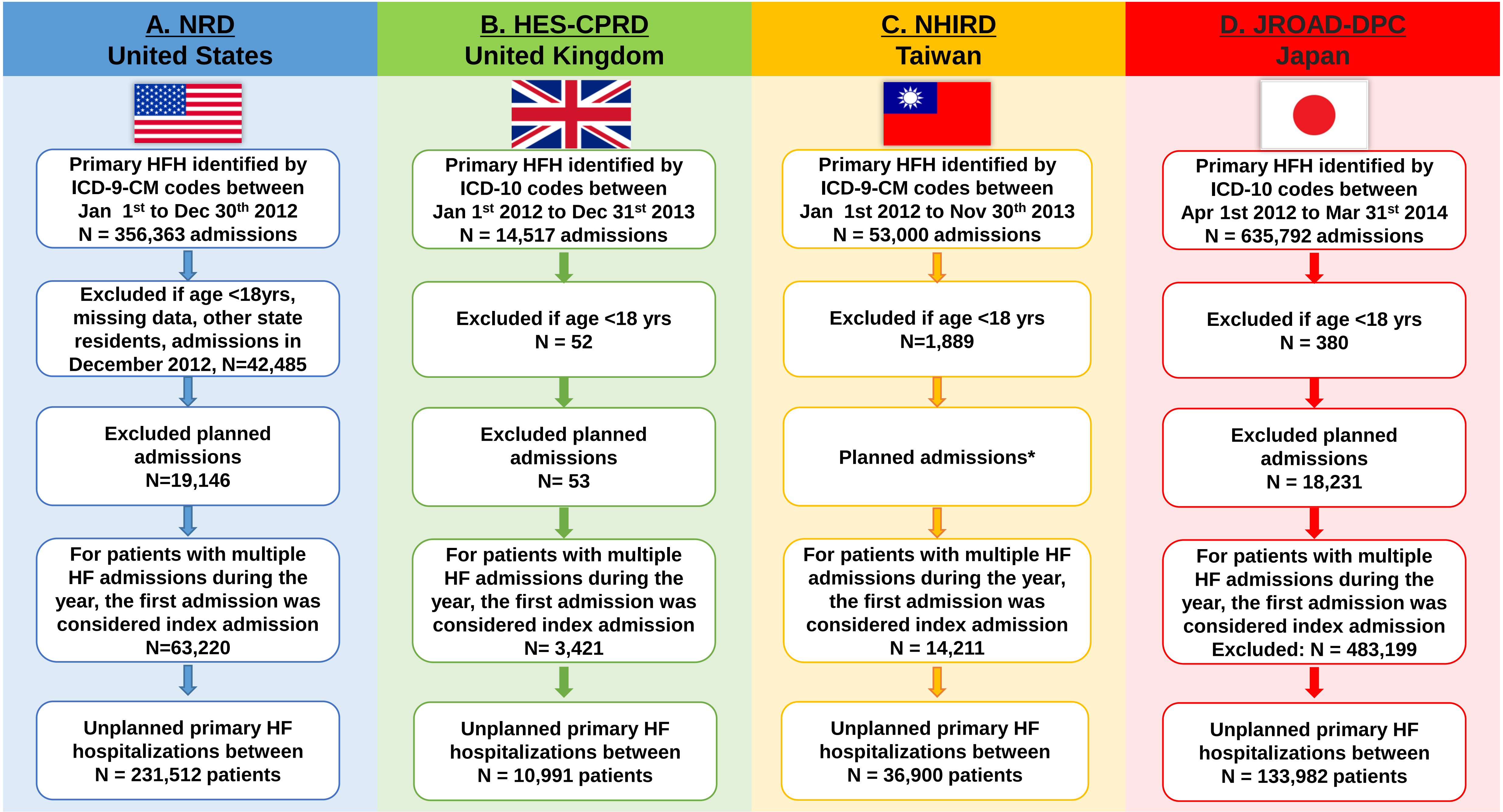


Figure 2. HF Hospitalisations Classified by Age Group in the USA, UK, Taiwan and Japan

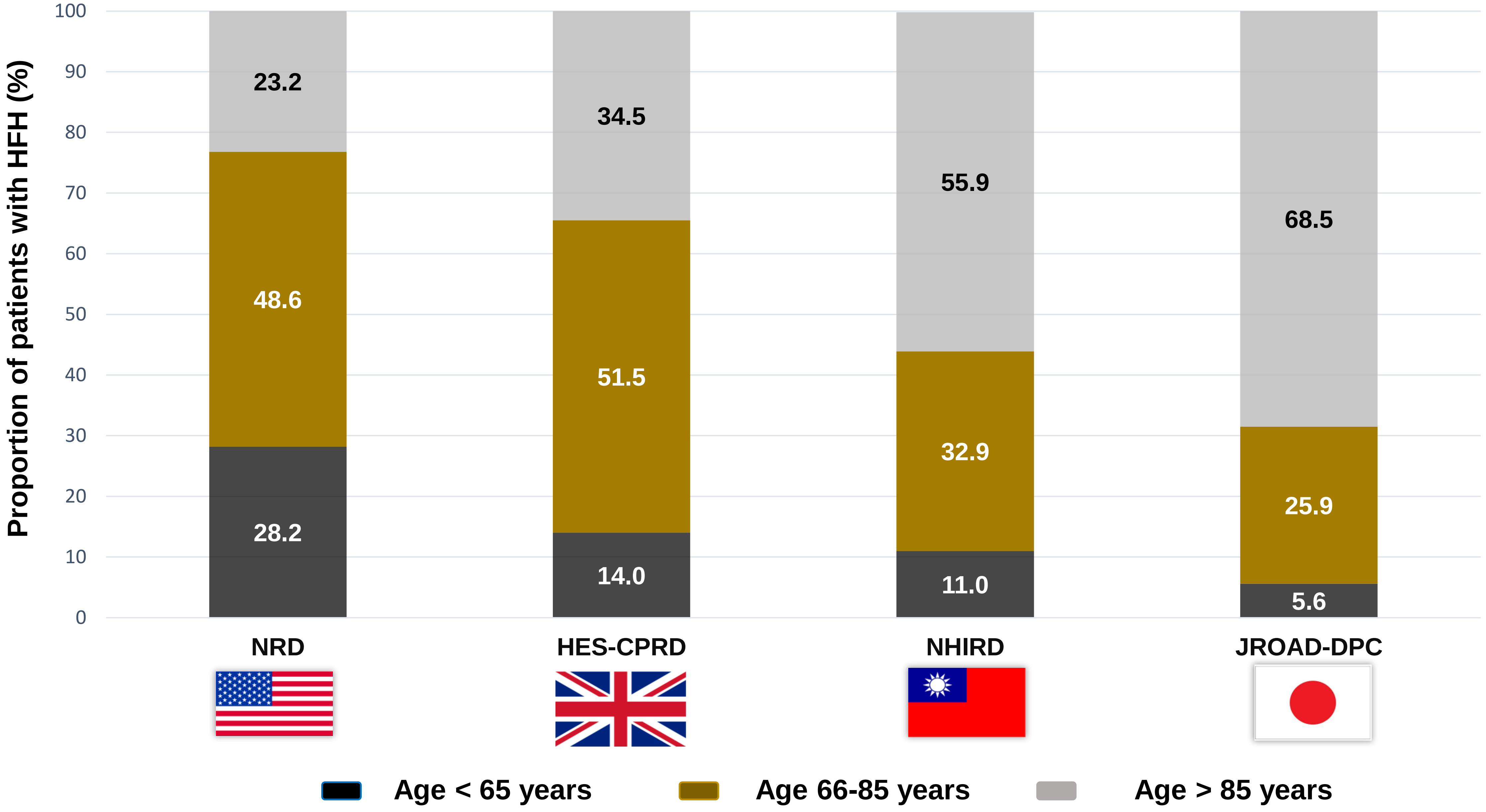


Figure 3. (A-B) Adjusted Differences In-hospital Mortality and (C-D) 30 day Readmissions in the UK and Japan Using Multivariable Logistic Regression and Inverse Probability Treatment Weighting (USA as the Reference Population)

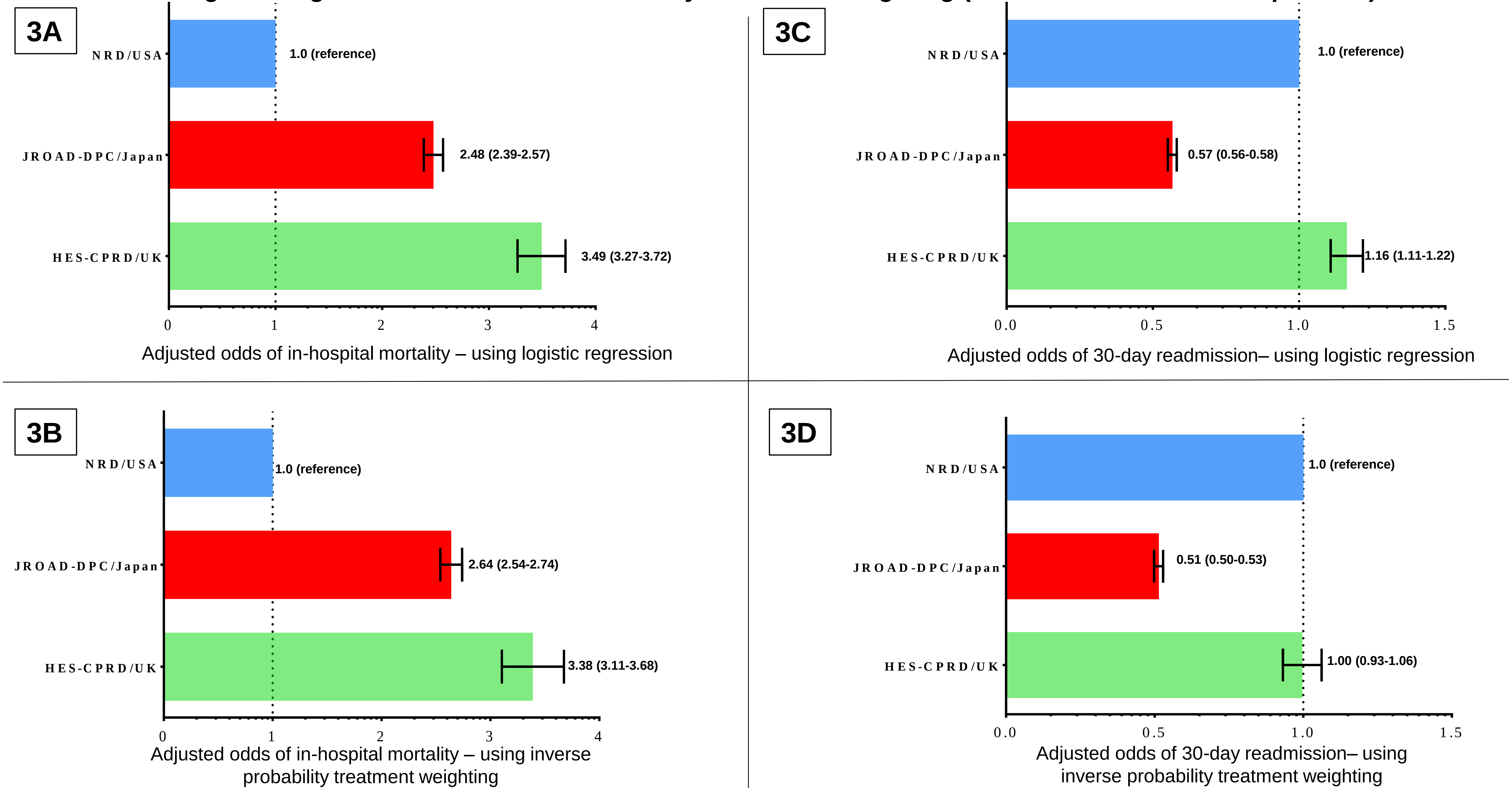


Figure 4. Factors Predicting In-hospital Mortality in the US, UK, Taiwan and Japan

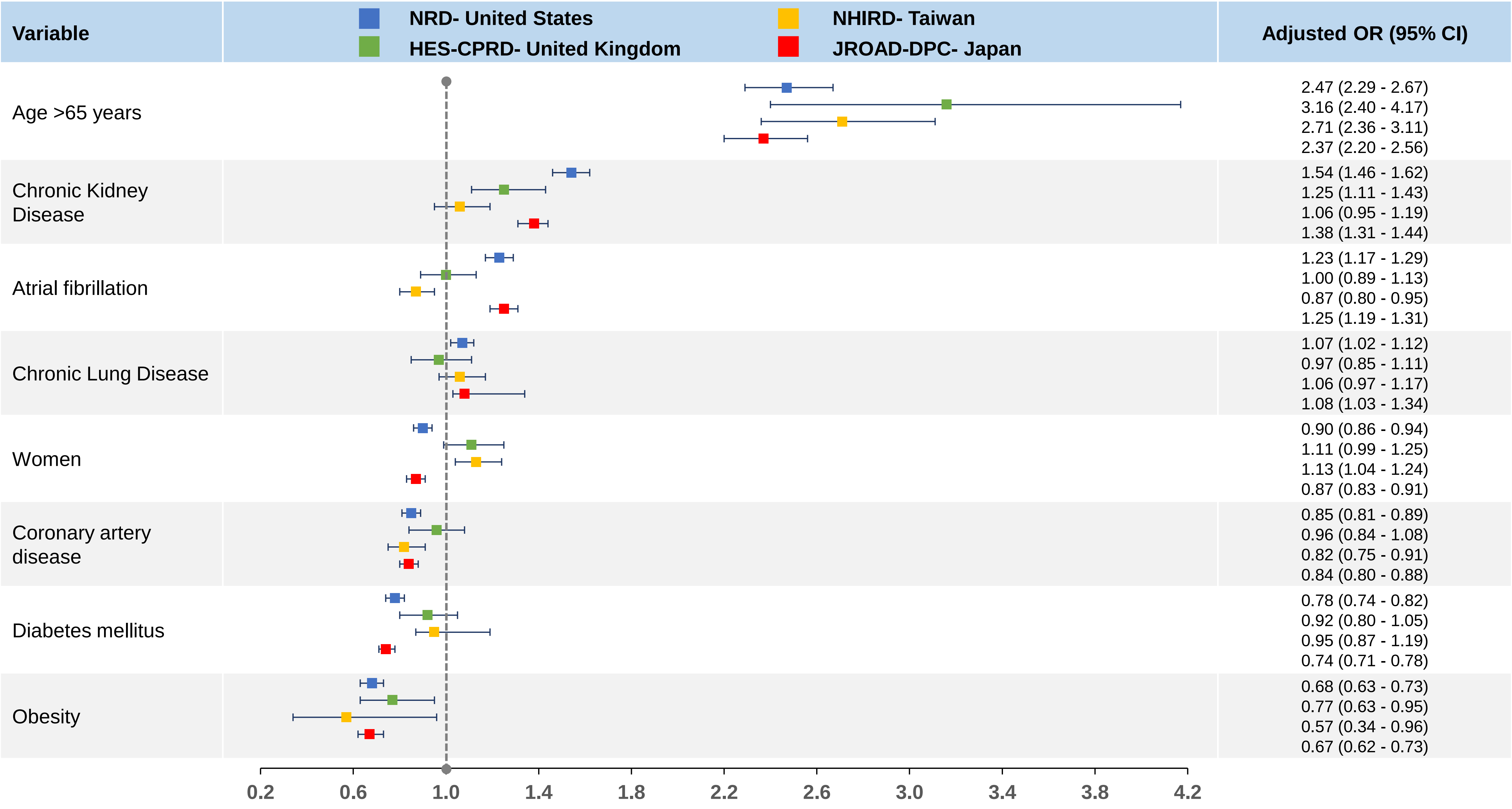
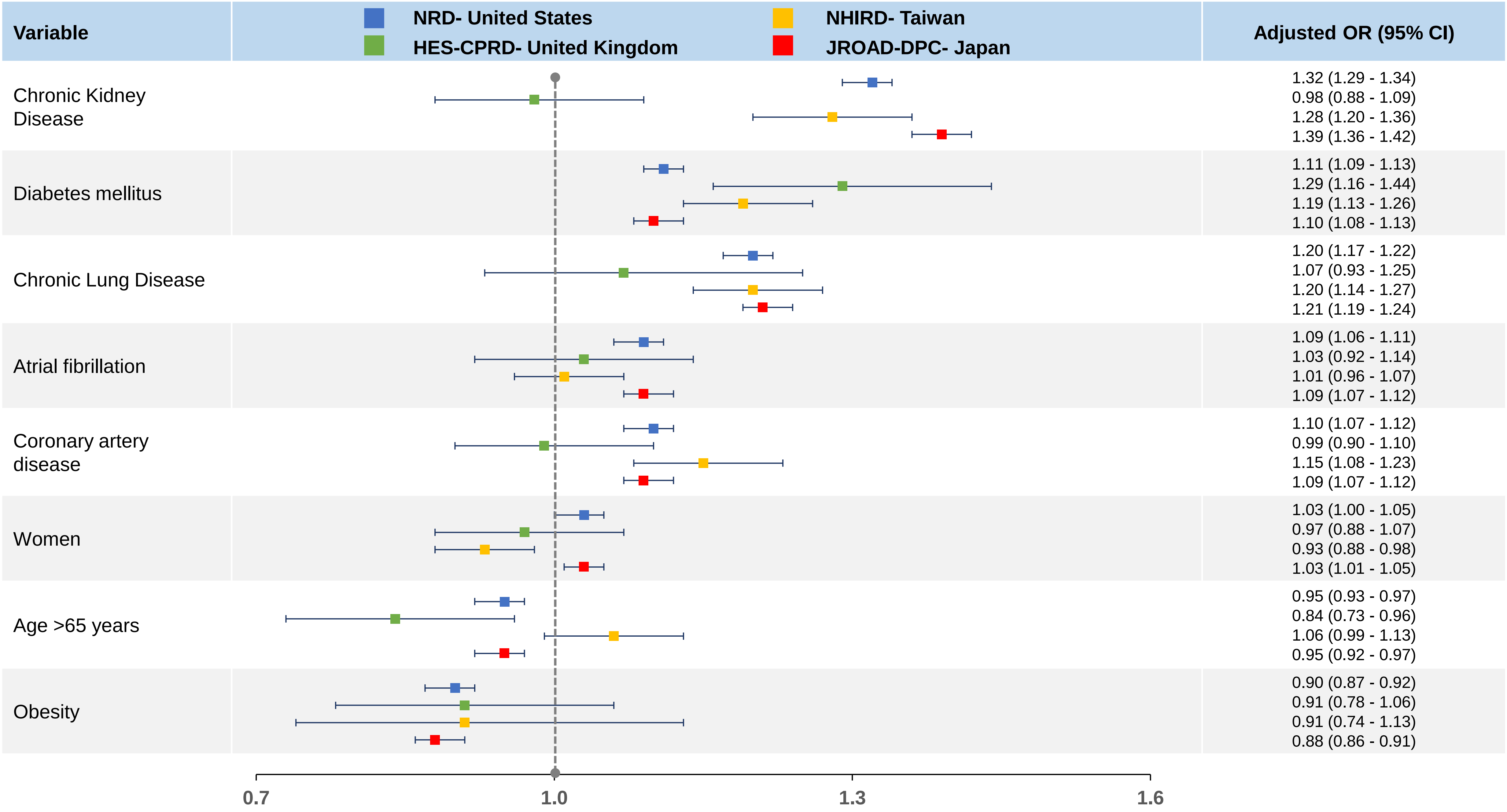


Figure 5. Factors Predicting 30-day Readmission in USA, UK, Taiwan and Japan



Central Illustration: Summary of All Outcomes in Patients with HFH in the USA, UK, Taiwan and Japan

Highest to Lowest	1	2	3	4
Hospitalizations for HF, per 100,000 people	USA	UK	Japan	Taiwan
Length of hospital stay, median	Japan	Taiwan	UK	USA
In-patient health care resource utilization	Japan	Taiwan	USA	UK
In-hospital mortality				
Crude rates, per 100 hospitalisations for HF	UK	Japan	Taiwan	USA
Age standardized rates, per 100 hospitalisations for HF	Japan	UK	Taiwan	USA
Sensitivity analyses; excluding patients discharged within 24 hours*	UK	Japan	Taiwan	USA
Adjusted odds**	UK	Japan	USA	
Adjusted odds among elderly (age > 65)	UK	Taiwan	USA	Japan
30-day readmission				
Crude rates, per 100 discharges	USA	UK	Taiwan	Japan
Adjusted odds**	USA	UK	Japan	
Adjusted odds among elderly (age > 65)	Taiwan	Japan	USA	UK