Comparing inpatient costs of heart failure admissions for patients with reduced and preserved ejection fraction with or without type 2 diabetes

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Objective Both heart failure (HF) and diabetes mellitus (DM) account for major healthcare expenditures. We evaluated inpatient expenditures and cost drivers in patients admitted with HF with and without DM.

Methods We created a retrospective cohort of acutely decompensated HF patients, using linked data from cost accounting systems and electronic medical records. We stratified patients by LVEF into reduced ejection fraction (HFrEF, LVEF $\leq 40\%$) and preserved ejection fraction (HFpEF, LVEF $>40\%$) groups and by DM status at admission.

Results Our population had 544 people: 285 HFrEF patients (43.5% with DM) and 259 HFpEF patients (43.6% with DM). Patients with HFrEF and DM had the longest hospital stay (5.10 ± 5.21 days). Patients with HFrEF and DM had the highest hospitalization cost (\$11 576 $\pm$ 15 818). HFrEF and HFpEF patients with DM had the highest cost, and cost per day alive was highest for HFpEF patients with DM [\$3153 (95% CI 2332, 4262)].

Conclusion Overall cost was higher for patients with DM, whether or not they were admitted with acute HF due to HFrEF or HFpEF. Cost per day alive for patients with DM continued to exceed corresponding costs for patients without DM, with HFpEF patients with DM having the highest cost. *Cardiovasc Endocrinol Metab* 9: 17–23 Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved.

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Keywords: diabetes, healthcare costs, health economics, heart failure, hospitalizations, type 2 diabetes

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Introduction

Despite recent advances in medical and device therapies, heart failure (HF) remains a highly prevalent and fatal disease associated with significant morbidity and cost to the healthcare system [1–3]. It is estimated that over 6.5 million adults in the United States (US) currently have HF and with an aging population, and the prevalence is expected to continue to increase for the foreseeable future [1,2,4]. Although HF survival rates have improved, mortality rates remain high at approximately 50% within 5 years following initial diagnosis [2,3]. HF readmission rates are also high, with approximately 25% of patients requiring hospital readmission within 30 days of discharge [5–7]. In 2012, total direct medical costs for HF totaled \$21 billion with projections of more than \$53 billion by 2030 [8]. As a consequence, there is increased interest in understanding which HF populations may be contributing most to these costs.

Patients with HF are a heterogeneous group with at least two distinct subtypes, namely, patients with reduced ejection fraction (HFrEF) and patients with preserved

ejection fraction (HFpEF) [9,10]. Each subtype accounts for about half of all patients with HF, although these proportions vary by population [11,12]. Prior studies have shown HFpEF patients have a wider age range and higher comorbidity burden compared to HFrEF patients [10,13]. In the general population, patients with HFpEF are usually older, have a higher proportion of women, and with higher prevalence of comorbidities such as obesity, coronary artery disease, diabetes mellitus (DM), atrial fibrillation, hypertension, and hyperlipidemia [9,10]. Because of this heterogeneity, incurred hospital expenditures depend on the type of HF, making this information important to payers and other decision makers [13,14].

Having clinical DM markedly increases the likelihood of developing HF [15–17]. In addition, DM rates among patients admitted to the hospital with HF are as high as 42% [18]. The number of US adults aged 18 years or older living with diagnosed DM has increased rapidly from 5.5 million in the 1980s to over 21.9 million in 2014 [19]. In 2017, due to the increasing prevalence in US, DM resulted in an estimated cost of \$327 billion (\$237 billion in direct costs and \$90 billion in reduced productivity) [20]. On average, medical expenditures for patients with DM exceed corresponding expenditures for those without DM by a factor of 2.3. In addition to medical

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costs, patients with DM incur substantial costs due to reduced and lost productivity and DM-induced disabilities. Furthermore, population-wide economic costs for DM increased by 26% during the 5 years from 2012 to 2017 [20].

Although prior research has evaluated inpatient expenditures and cost drivers for patients with HF [21] and patients with DM [22] independently, few studies have evaluated expenditures, cost drivers, and the relationship between cost and length of hospital stay (LOS) for patients with HF by both subtype (HFrEF vs. HFpEF) and DM status. We therefore sought to evaluate inpatient expenditures and LOS for patients admitted to our hospital with acute decompensated HF.

Methods

Our prior article details the population and data collection methods [21]. Briefly, we created a retrospective cohort of consecutively admitted (index hospitalization only) acutely decompensated HF patients [coded with HF-related diagnosis-related group codes 291 (HF and shock with major complication or comorbidity), 292 (HF and shock with a complication or comorbidity), or 293 (HF and shock without a complication or comorbidity)], who were discharged between 1st October 2010 and 30th November 2013 (both dates inclusive). Each patient included was unique and we excluded subsequent hospitalizations for the same patient. We also excluded patients with prior heart transplant or prior left ventricular assist device placement because their costs cannot be generalized to a typical HF population.

For the present analyses, we stratified the cohort by left ventricular ejection fraction (LVEF) into a preserved ejection fraction (HFpEF) group (LVEF >40%) and a reduced ejection fraction (HFrEF) group (LVEF ≤40%), and by their DM status at admission. The LVEF threshold of 40% is typically used to designate patients in US as either HFrEF or HFpEF [7]. Since the European Society for Cardiology defines patients with LVEF between 41 and 49% as mid-range LVEF, we performed a sensitivity analysis that excluded these patients and instead defined HFpEF as LVEF >50% [23]. Combined with the DM status at admission, we had four distinct patient populations – HFrEF with DM, HFrEF without DM, HFpEF with DM, and HFpEF without DM.

We extracted cost information from the Tufts Medical Center cost accounting system, linking patient and admission information to their electronic medical record using medical record numbers and date of admission. We reported total costs, costs by category [21], and total costs per day for the index hospitalization by type of HF (HFrEF vs. HFpEF) and DM status. Direct cost components included room and board (room and board medical/surgical, room and board ICU, and dietary/housekeeping services), diagnostics (core blood laboratory, radiation

oncology, radiology, MRI, and other ancillary diagnostic testing), therapies (operating room, electrophysiology laboratory, and cardiac catheterization laboratory), pharmacy, and others (blood bank and emergency department). We used the medical care services component of the US Consumer Price Index to adjust all costs to 2015 US dollars. Data on reimbursements were not available through the cost accounting system.

We summarized patient demographics, clinical and laboratory characteristics, medications, and discharge disposition for both the total cohort and for each of the four HF subgroups separately. We reported mean and median values for continuous variables and counts with percentages for categorical data. We used Student's *t*-test for continuous data and the χ^2 test or Fisher's exact test for categorical data to compare the HF subgroups. For highly skewed continuous data, we log-transformed the data and then used Student's *t*-test. All tests were two-sided, with the *a priori* significance level set at 0.05.

Since costs tend to be skewed, we used generalized linear models with gamma distribution and log-link functions in our multivariable regressions, where costs were the outcome. We adjusted for patient demographics, prior HF history, HF etiology, and whether awaiting heart transplant to estimate adjusted total costs, costs by category, and total costs per day alive for each HF patient subgroup. We selected adjustment variables based on *a priori* clinical knowledge of what factors would likely affect medical costs, LOS, or both [24,25].

The Tufts Medical Center Institutional Review Board approved this study and waived the requirement for written patient consent because of the study's retrospective nature. We used SAS version 9.4 software (SAS Institute Inc., Cary, North Carolina, USA) and STATA (Stata Statistical Software: Release 12, version College Station, Texas: StataCorp LP) to perform all statistical analyses.

Results

Our population had 544 people, of whom 285 (52.4%) were HFrEF patients (124 or 43.5% with DM) and 259 (47.6%) were HFpEF patients (113 or 43.6% with DM). HFpEF patients tended to be older and more likely to be female (Table 1). Among all patients with HF, patients with DM were more likely to have higher BMI and to have comorbidities (hypertension, hyperlipidemia, depression, and dialysis). Patients with DM were also more likely to have a prior history of HF at admission and ischemic etiology for HF. Patients with HFpEF had significantly higher SBP, with HFpEF with DM patients having the highest mean SBP values. A much higher proportion of HFrEF patients had defibrillator/pacemakers than did HFpEF patients, and were much more likely to be listed for heart transplant. BNP levels were much higher among HFrEF patients, with highest mean values seen among those without DM. Sensitivity analyses that

Table 1 Study population characteristics, overall, and for left ventricular ejection fraction and diabetes mellitus subgroups

Characteristics	Total population N = 544	HFpEF (LVEF ≤ 40)		HFpEF (LVEF > 40)		P value
		DM	No DM	DM	No DM	
Demographics						
Age*	71.04 (15.13)	67.73 (13.93)	67.24 (17.26)	73.91 (10.67)	75.84 (14.85)	<0.0001
Female sex	238 (44%)	45 (36%)	42 (26%)	65 (58%)	86 (59%)	<0.0001
Race						
White	380 (70.63%)	79 (64.23%)	123 (77.85%)	69 (62.16%)	109 (74.66%)	<0.0001
Black	59 (10.97%)	22 (17.89%)	9 (5.70%)	17 (15.32%)	11 (7.53%)	
Asian	72 (13.38%)	10 (8.13%)	16 (10.13%)	22 (19.82%)	24 (16.44%)	
Other	27 (5.02%)	12 (9.76%)	10 (6.33%)	3 (2.70%)	2 (1.37%)	
Smoking history						
Current smoker	52 (9.58%)	12 (9.76%)	15 (9.32%)	11 (9.73%)	14 (9.59%)	0.999
Non-smoker ^a	491 (90.42%)	111 (90.24%)	146 (90.68%)	102 (90.27%)	132 (90.41%)	
BMI*	29.65 (8.39)	31.05 (7.49)	27.04 (7.64)	32.91 (8.61)	28.81 (8.71)	<0.0001
Chronic conditions						
Atrial fibrillation or flutter at admission	242 (44.49%)	43 (34.68%)	69 (42.86%)	61 (53.98%)	69 (47.26%)	0.02
Hypertension	398 (73.30%)	92 (74.80%)	98 (60.87%)	98 (86.75%)	110 (75.34%)	<0.0001
Hyperlipidemia	272 (50.00%)	76 (61.29%)	72 (44.72%)	72 (63.72%)	52 (35.62%)	<0.0001
COPD	119 (21.96%)	18 (14.63%)	29 (18.13%)	32 (28.30%)	40 (27.40%)	0.02
Cancer	52 (9.56%)	9 (7.26%)	17 (10.56%)	8 (7.08%)	18 (12.33%)	0.4
Depression (currently on medication)	109 (20.15%)	29 (23.58%)	23 (14.37%)	27 (23.89%)	30 (20.69%)	0.2
Renal dialysis	29 (5.33%)	8 (6.45%)	4 (2.48%)	10 (8.85%)	7 (4.79%)	0.1
Ventricular tachycardia	37 (6.80%)	15 (12.10%)	20 (12.42%)	1 (0.88%)	1 (0.68%)	<0.0001
Prior stroke/TIA	73 (13.42%)	12 (9.68%)	17 (10.56%)	25 (22.12%)	19 (13.01%)	0.02
Previous history of heart failure	369 (67.33%)	98 (79.03%)	118 (73.29%)	68 (60.18%)	85 (58.22%)	<0.0001
	15 (2.76%)	5 (4.03%)	9 (5.59%)	0 (0.00%)	1 (0.68%)	0.006
Listed for heart transplant						
Heart failure etiology						
Ischemic	288 (54.14%)	88 (72.13%)	87 (54.37%)	60 (54.05%)	53 (38.13%)	<0.0001
Idiopathic dilated CM	128 (24.06%)	20 (16.39%)	50 (31.25%)	24 (21.62%)	34 (24.46%)	
Other	116 (21.80%)	14 (11.48%)	23 (14.37%)	27 (24.32%)	52 (37.41%)	
Blood pressure						
Blood pressure, systolic at admit (mm Hg)*	130.46 (24.87)	128.49 (22.96)	122.02 (23.83)	139.81 (25.63)	134.19 (23.85)	<0.0001
Blood pressure, diastolic at admit (mm Hg)*	69.51 (16.18)	71.33 (16.61)	71.50 (15.79)	67.73 (16.39)	67.19 (15.79)	0.04
Medications on admission						
ACE inhibitors/ARBs	264 (48.53%)	68 (54.84%)	89 (55.28%)	55 (48.67%)	52 (35.62%)	0.002
Mineralocorticoid receptor antagonist	73 (13.42%)	27 (21.77%)	34 (21.12%)	8 (7.08%)	4 (2.74%)	<0.0001
Statin	319 (58.64%)	94 (75.81%)	75 (46.58%)	78 (69.03%)	72 (49.32%)	<0.0001
Beta blockers (any)	411 (75.55%)	103 (83.06%)	119 (73.91%)	86 (76.11%)	103 (70.55%)	0.1
Loop Diuretics	347 (63.79%)	94 (75.81%)	102 (63.35%)	68 (60.18%)	83 (56.86%)	0.01
Laboratory values						
Serum sodium (mEq/l)*	137.47 (4.35)	137.25 (4.15)	137.12 (4.29)	137.62 (4.82)	137.95 (4.19)	0.4
Creatinine (mg/dl)*	1.64 (1.26)	1.74 (1.03)	1.56 (1.09)	1.88 (1.64)	1.48 (1.26)	0.05
Hemoglobin (g/dl)*	11.54 (2.18)	11.52 (2.30)	12.07 (2.21)	10.87 (2.04)	11.47 (2.01)	0.0001
Hematocrit (%)*	35.46 (6.17)	35.37 (6.71)	36.87 (6.20)	33.88 (5.96)	35.18 (5.52)	0.001
BNP level (peak pg/ml value during admission)*	969.71 (1047.97)	1205.57 (1217.58)	1398.79 (1218.61)	637.92 (671.54)	606.17 (692.23)	<0.0001
Discharged home	398 (73%)	90 (73%)	122 (76%)	79 (70%)	107 (73%)	0.8
LVEF	39.37 (19.02)	24.07 (10.08)	22.64 (10.17)	57.26 (6.54)	56.99 (6.92)	<0.0001

Frequency (percentages) reported for categorical variable and mean (±SD) reported for continuous variables (*indicates continuous variables).

Twenty patients from the study cohort had a missing value for LVEF.

ACE, angiotensin converting enzyme; ARBs, Angiotensin II receptor blockers; BNP, brain natriuretic peptide; CM, cardiomyopathy; CRT, cardiac resynchronization therapy; COPD, chronic obstructive pulmonary disease; HF, heart failure; HFpEF, reduced ejection fraction; HR, heart rate; ICD, implantable cardiac defibrillator; LVEF, left ventricular ejection fraction; TIA, transient ischemic attack.

^aIncludes past-smokers, nonsmokers, and those with unknown smoking status.

Fig. 1

Note: costs were adjusted for Age, Gender, Race, BMI, Previous history of heart failure, Etiology of heart failure and Awaiting Heart Transplant.

All costs adjusted to US\$ 2015 values and rounded up to the nearest US\$.

Hospitalization costs by category. Note: costs were adjusted for age, gender, race, BMI, previous history of heart failure, etiology of heart failure, and awaiting heart transplant. All costs adjusted to US\$ 2015 values and rounded up to the nearest US\$.

Table 3 Hospitalization costs by category, stratified by diabetes status and heart failure subtypes

Cost contributor	HFrEF (LVEF ≤ 40)		HFpEF (LVEF > 40)	
	DM	No DM	DM	No DM ^a
Total cost	14 950 (6163, 36 267)	11 022 (4648, 26 140)	13 715 (5354, 35 135)	10 602 (4187, 26 842)
Room and board expenses	5547 (2171, 14 171)	4108 (1644, 10 265)	4802 (1771, 13 021)	3684 (1371, 9899)
Diagnostic	1073 (492, 2339)	838 (392, 1790)	1,015 (443, 2325)	836 (371, 1886)
Therapies	469 (48, 4600)	304 (35, 2658)	675 (65, 6998)	377 (37, 3844)
Pharmacy	653 (178, 2391)	399 (113, 1412)	530 (133, 2116)	424 (109, 1649)
Other expenses	1109 (473, 2600)	1025 (446, 2355)	1,223 (494, 3029)	1089 (447, 2652)
Total cost per day alive	2836 (2130, 3776)	2709 (2049, 3582)	3153 (2332, 4262)	2853 (2116, 3846)

CI, confidence interval; DM, diabetes mellitus; HF, heart failure; HFrEF, reduced ejection fraction; LVEF, left ventricular ejection fraction.

Values show mean (95% CI). All costs adjusted to US\$ 2015 values and rounded up to the nearest US\$.

Adjusted for age, gender, race, BMI, previous history of heart failure, etiology of heart failure and awaiting heart transplant.

^aResults obtained from Gamma regression.

Discussion

Our present study aimed to describe the costs associated with an index acute HF hospitalization stratified by DM and HFrEF vs. HFpEF status. We found that overall costs were higher for patients with DM regardless of HFrEF vs. HFpEF status at admission. As we previously observed, LOS was a major driver for overall index admission cost [21]. Interestingly, cost per day alive (i.e. cost adjusted for LOS) for patients with DM exceeded corresponding costs for patients without DM, with the

highest cost per day observed for HFpEF patients with DM. These results extend our prior findings and suggest comorbidities like DM may increase costs for patients with HF.

Patients with HF have been broadly divided into two distinct groups based on their LVEF. The ACC/AHA Guidelines define HFrEF patients to include those individuals with LVEF of ≤40% and HFpEF patients to include those individuals with LVEF ≥50% [7]. Approximately half the patients with HF have HFpEF,

although evidence-based treatment strategies for this group are limited when compared to the treatment strategies for HFrEF patients [9–12]. The cutoff of $\leq 40\%$ has traditionally been used for the definition of HFrEF, for instance, in recent clinical trials examining HF patients [26].

Patients with HF with a LVEF from 41 to 49% fall into a borderline or intermediate group and appear to have characteristics, treatment patterns, and outcomes similar to those of patients with HFpEF [7,23]. Based on this information, we defined our HFrEF group as having a LVEF $\leq 40\%$ and our HFpEF group as having a LVEF $> 40\%$. To better understand the behavior of the intermediate ejection fraction group in our study, we also performed several sensitivity analyses defining HFpEF to include patients with LVEF $\geq 50\%$ and HFrEF, but this alternative definition did not substantially influence our results.

DM is a major comorbidity and risk factor for the development of HF [15–17]. In the Framingham Study, DM was an independent risk factor for HF with men with DM having a 2.4-fold and women with DM a five-fold higher risk of HF [15]. In addition, 42% of patients admitted to the hospital in the OPTIMIZE-HF Registry were found to have DM as a significant comorbidity [18]. Our study had similar findings with an observed prevalence for DM in our acute HF population of 44% in both the HFrEF and HFpEF groups. In addition, HF patients with DM have been shown to have a higher mortality and readmission rates when compared to patients without DM [27,28]. These data taken together suggest a potential increased cost and economic burden for patients with HF and DM consistent with our study findings, demonstrating increased cost associated with the diabetic subgroup. In a recent study, the choice of blood glucose-lowering medication also appears to play a major role in the development of HF in patients with DM [29]. Some diabetic drugs (i.e. saxagliptin and rosiglitazone) have been associated with an increased risk of developing HF and HF hospitalizations, whereas others (i.e. dapagliflozin, ertugliflozin, empagliflozin, and canagliflozin) have decreased these events [30]. The sodium glucose cotransporter-2 inhibitors like empagliflozin and canagliflozin provide a new therapeutic strategy that may have an impact on cardiovascular outcomes for patients with HF in addition to the currently approved HF medications [29,30]. Whether these newer diabetic agents will have an impact on decreasing the cost of caring for patients with HF and DM is still to be determined.

Limitations

This study is subject to the methodological limitations typical of any retrospective cohort study. The cohort and costs are from Tufts Medical Center, an academic teaching hospital, and may not be representative of

other healthcare settings, especially community-based hospitals. This is also a relatively small single-center study. Despite this size limitation, the analysis incorporated detailed data on both clinical factors and costs by hospitalization component. Although this study's cost data comprehensively account for care provided during an inpatient hospitalization at Tufts Medical Center, no attending physician reimbursement were available as part of this study. Inclusion of professional (physician) fees would be expected to add approximately 20% to inpatient costs [31].

Conclusion

We found that overall costs were higher for patients with DM, whether or not they were admitted with acute HF due to HFrEF or HFpEF. When we indexed admissions to account for LOS, we observed that cost per day alive for patients with DM continued to exceed corresponding costs for patients without DM, with the highest costs observed among HFpEF patients with DM. These findings extend our prior investigations and have implications on our understanding of the economic impact of certain HF comorbidities such as DM.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

- 1 Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, *et al.*; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2017 update: a report from the American heart association. *Circulation* 2017; **135**:e146–e603.
- 2 Levy D, Kenchaiah S, Larson MG, Benjamin EJ, Kupka MJ, Ho KK, *et al.* Long-term trends in the incidence of and survival with heart failure. *N Engl J Med* 2002; **347**:1397–1402.
- 3 Roger VL, Weston SA, Redfield MM, Hellermann-Homan JP, Killian J, Yawn BP, Jacobsen SJ. Trends in heart failure incidence and survival in a community-based population. *JAMA* 2004; **292**:344–350.
- 4 Curtis LH, Whellan DJ, Hammill BG, Hernandez AF, Anstrom KJ, Shea AM, Schulman KA. Incidence and prevalence of heart failure in elderly persons, 1994–2003. *Arch Intern Med* 2008; **168**:418–424.
- 5 Fang J, Mensah GA, Croft JB, Keenan NL. Heart failure-related hospitalization in the U.S., 1979 to 2004. *J Am Coll Cardiol* 2008; **52**:428–434.
- 6 Krumholz HM, Merrill AR, Schone EM, Schreiner GC, Chen J, Bradley EH, *et al.* Patterns of hospital performance in acute myocardial infarction and heart failure 30-day mortality and readmission. *Circ Cardiovasc Qual Outcomes* 2009; **2**:407–413.
- 7 Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, *et al.*; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American college of cardiology foundation/American heart association task force on practice guidelines. *J Am Coll Cardiol* 2013; **62**:e147–e239.
- 8 Heidenreich PA, Albert NM, Allen LA, Blumke DA, Butler J, Fonarow GC, *et al.*; American Heart Association Advocacy Coordinating Committee; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Stroke Council. Forecasting the impact of heart failure in the united states: a policy statement from the American heart association. *Circ Heart Fail* 2013; **6**:606–619.
- 9 Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med* 2006; **355**:251–259.
- 10 Steinberg BA, Zhao X, Heidenreich PA, Peterson ED, Bhatt DL, Cannon CP, *et al.*; Get With the Guidelines Scientific Advisory Committee and

- Investigators. Trends in patients hospitalized with heart failure and preserved left ventricular ejection fraction: prevalence, therapies, and outcomes. *Circulation* 2012; **126**:65–75.
- 11 Savarese G, Lund LH. Global public health burden of heart failure. *Card Fail Rev* 2017; **3**:7–11.
 - 12 Tiller D, Russ M, Greiser KH, Nuding S, Ebel H, Kluttig A, *et al.* Prevalence of symptomatic heart failure with reduced and with normal ejection fraction in an elderly general population—the CARLA study. *PLoS One* 2013; **8**:e59225.
 - 13 Lam CS, Donal E, Kraigher-Krainer E, Vasan RS. Epidemiology and clinical course of heart failure with preserved ejection fraction. *Eur J Heart Fail* 2011; **13**:18–28.
 - 14 Bhuiyan T, Maurer MS. Heart failure with preserved ejection fraction: persistent diagnosis, therapeutic enigma. *Curr Cardiovasc Risk Rep* 2011; **5**:440–449.
 - 15 Kannel WB, Hjortland M, Castelli WP. Role of diabetes in congestive heart failure: the Framingham study. *Am J Cardiol* 1974; **34**:29–34.
 - 16 He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. Risk factors for congestive heart failure in US men and women: NHANES I epidemiologic follow-up study. *Arch Intern Med* 2001; **161**:996–1002.
 - 17 Nichols GA, Gullion CM, Koro CE, Ephross SA, Brown JB. The incidence of congestive heart failure in type 2 diabetes: an update. *Diabetes Care* 2004; **27**:1879–1884.
 - 18 Greenberg BH, Abraham WT, Albert NM, Chiswell K, Clare R, Stough WG, *et al.* Influence of diabetes on characteristics and outcomes in patients hospitalized with heart failure: a report from the organized program to initiate life-saving treatment in hospitalized patients with heart failure (OPTIMIZE-HF). *Am Heart J* 2007; **154**:277.e1–277.e8.
 - 19 Lin J, Thompson TJ, Cheng YJ, Zhuo X, Zhang P, Gregg E, Rolka DB. Projection of the future diabetes burden in the United States through 2060. *Popul Health Metr* 2018; **16**:9.
 - 20 Economic costs of diabetes in the U.S. in 2017. *Diabetes Care* 2018; **41**:917–928.
 - 21 Olchanski N, Vest AR, Cohen JT, Neumann PJ, DeNofrio D. Cost comparison across heart failure patients with reduced and preserved ejection fractions: analyses of inpatient decompensated heart failure admissions. *Int J Cardiol* 2018; **261**:103–108.
 - 22 Ozieh MN, Bishu KG, Dismuke CE, Egede LE. Trends in health care expenditure in U.S. Adults with diabetes: 2002–2011. *Diabetes Care* 2015; **38**:1844–1851.
 - 23 Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, *et al.*; ESC Scientific Document Group. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European society of cardiology (ESC) developed with the special contribution of the heart failure association (HFA) of the ESC. *Eur Heart J* 2016; **37**:2129–2200.
 - 24 Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, *et al.*; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2014 update: a report from the American heart association. *Circulation* 2014; **129**:e28–e292.
 - 25 Whellan DJ, Zhao X, Hernandez AF, Liang L, Peterson ED, Bhatt DL, *et al.* Predictors of hospital length of stay in heart failure: findings from get with the guidelines. *J Card Fail* 2011; **17**:649–656.
 - 26 McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, *et al.*; PARADIGM-HF Investigators and Committees. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med* 2014; **371**:993–1004.
 - 27 Shindler DM, Kostis JB, Yusuf S, Quinones MA, Pitt B, Stewart D, *et al.* Diabetes mellitus, a predictor of morbidity and mortality in the studies of left ventricular dysfunction (SOLVD) trials and registry. *Am J Cardiol* 1996; **77**:1017–1020.
 - 28 Carr AA, Kowey PR, Devereux RB, Brenner BM, Dahlöf B, Ibsen H, *et al.* Hospitalizations for new heart failure among subjects with diabetes mellitus in the RENAAL and LIFE studies. *Am J Cardiol* 2005; **96**:1530–1536.
 - 29 Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, *et al.*; EMPA-REG OUTCOME Investigators. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med* 2015; **373**:2117–2128.
 - 30 Fitchett DH, Udel JA, Inzucchi SE. Heart failure outcomes in clinical trials of glucose-lowering agents in patients with diabetes. *Eur J Heart Fail* 2017; **19**:43–53.
 - 31 Peterson C, Xu L, Florence C, Grosse SD, Annett JL. Professional fee ratios for US hospital discharge data. *Med Care* 2015; **53**:840–849.