The Economic Impact of Mitral Regurgitation on Patients With Medically Managed Heart Failure

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The objective of this study was to quantify the financial healthcare burden of mitral regurgitation (MR) on medically managed heart failure (HF) patients. Data from the Truven Health MarketScan Commercial Claims and Medicare Supplemental Databases were analyzed. Included patients had a minimum of 1 inpatient or 2 outpatient claims for HF with a 6-month preperiod (baseline). A 6-month postperiod (landmark) after HF index was used to capture MR diagnosis and severity. Following the landmark period, patients had to have 12 months of continuous medical and prescription drug plan enrollment with at least 2 records of HF medication refills. A therapeutic intensity score was calculated based on HF medication usage. Medically managed HF patients were separated into 3 cohorts: without MR (no MR), insignificant MR (iMR), and significant MR (sMR). Healthcare utilization and all-cause expenditures were modeled to quantify the burden of MR. All models controlled for baseline demographics, co-morbid conditions, and HF therapeutic intensity. Medically managed incident HF patients with sMR had significantly more hospital days (1.91 vs 1.72 days; $p = 0.0096$) and annual expenditures ($23,988 vs $21,530; $p < 0.0001$) compared with no MR patients. No differences were identified when comparing iMR and no MR. When evaluating HF admissions, sMR patients had an estimated 50% greater HF admissions rate (0.036 vs 0.024; $p < 0.0001$) compared with no MR patients. Additionally, HF admits for iMR were 23% more than those with no MR (0.029 vs 0.024; $p = 0.0064$). In conclusion, evidence of MR in retrospective claims significantly increases the healthcare impact of medically managed HF patients. Both utilization and financial burden is more pronounced when MR is clinically significant. **(Am J Cardiol 2019;124:1226−1231)**

Heart failure (HF) is a prevalent condition associated with consistently high morbidity and mortality rates, frequent hospitalizations, and a substantial clinical and economic burden that is projected to increase as the population ages and grows.[1−3] The incidence of newly-diagnosed HF in the United States stands at approximately 1 million cases per year,[1] and mortality remains unchanged.[2,3] Hospitalizations account for the largest contributor to treatment costs for cardiovascular disease.[2] Over half of the estimated $100.9 billion in direct costs in 2013 were hospital-related, with $55 billion attributed to hospital inpatient admissions and $6.3 billion to emergency department visits.[1] Additionally, the costs of cardiac medications in the United States, while not as significant as hospitalization, are exceedingly high at $9.6 billion per year (in 2013).[1] Published studies[4−6] demonstrate the negative impact of mitral regurgitation (MR) on HF outcomes in patients with left ventricular dysfunction,[4] HF and reduced ejection fraction,[5] and ischemic heart disease.[6] MR is the most common form of valvular heart disease in the United States and, like HF, is especially prevalent in elderly populations, affecting about 10% of people aged 75 years and older.[7−10] In secondary MR, the MV leaflets are morphologically normal, but there is inadequate leaflet coaptation due to left ventricular dilatation.[10−12] Secondary MR is more common, has a worse prognosis, and is more difficult to treat than primary MR.[9−13] The focus of this study was to estimate the economic impact of secondary MR on patients with newly-diagnosed, medically-managed HF.

Methods

Data from the Truven Health MarketScan Commercial Claims and Medicare Supplemental Databases from October 1, 2011, through September 30, 2016, were used in this analysis. These resources provide access to fully integrated, deidentified, individual-level healthcare claims data. The data set includes complete payment records (insurance payments and patient payments), specialty pharmacy and mail-order records for individuals covered by a variety of health plans throughout the United States. Data from individual patients are integrated from all provisions of care, maintaining all

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healthcare utilization and cost record connections at the patient level. This database is inclusive of 150 employers and 21 health plans, representing 130 unique national carriers.[14]

Eligible patients were restricted to the following enrollment criteria: an index HF-diagnosis, 12 months of enrollment (medical and pharmacy) before the index diagnosis, and 18 months of follow-up postindex. In the first 6 months postindex (landmark period), patients with HF were categorized by their MR diagnosis. The landmark period also allowed patients with newly-diagnosed HF to have medical therapy titration before the application of a therapeutic intensity score. Patients met the requirement of an index HF-diagnosis if they had 1 inpatient or at least 2 outpatient visits with HF diagnosis codes (Appendix A).[15] The following patients were excluded (1) age less than 18 years; (2) record of end-stage renal disease at any time; or (3) a record of any of the following during the 12 months pre- or during the landmark period: left ventricular assisted devices, heart transplantation, chordal rupture, mitral stenosis, rheumatic mitral insufficiency, rheumatic tricuspid insufficiency, or hospice or palliative care (Appendix B). Finally, investigators applied additional inclusion criteria of at least 2 medication fills for HF and enrollment during the 12 months following the landmark period. See Figure 1 for the Attrition Diagram.

HF patients meeting the criteria above were further divided into the following 3 cohorts based on MR-status (see Appendix C for MR coding detail): (1) no MR, (2) insignificant MR (iMR), and (3) clinically-significant MR (sMR). The no MR cohort was comprised of patients with a diagnosis of HF and no findings of MR at any time in the database. Patients with a diagnosis of MR, either at the index HF diagnosis or in the 6-month landmark period, were flagged as having MR and further subdivided by MR severity. Patients were defined as having sMR if they had any of the following indicators at index or during the landmark period (1) diagnosis of pulmonary hypertension or atrial fibrillation, (2) record of MR surgery, or (3) two or more echocardiograms during analysis period, which served as a proxy measure for clinical concern. Patients were excluded if they had a diagnosis of MR before index HF diagnosis or if first MR diagnosis occurred after the landmark period (see Appendix D for coding detail).

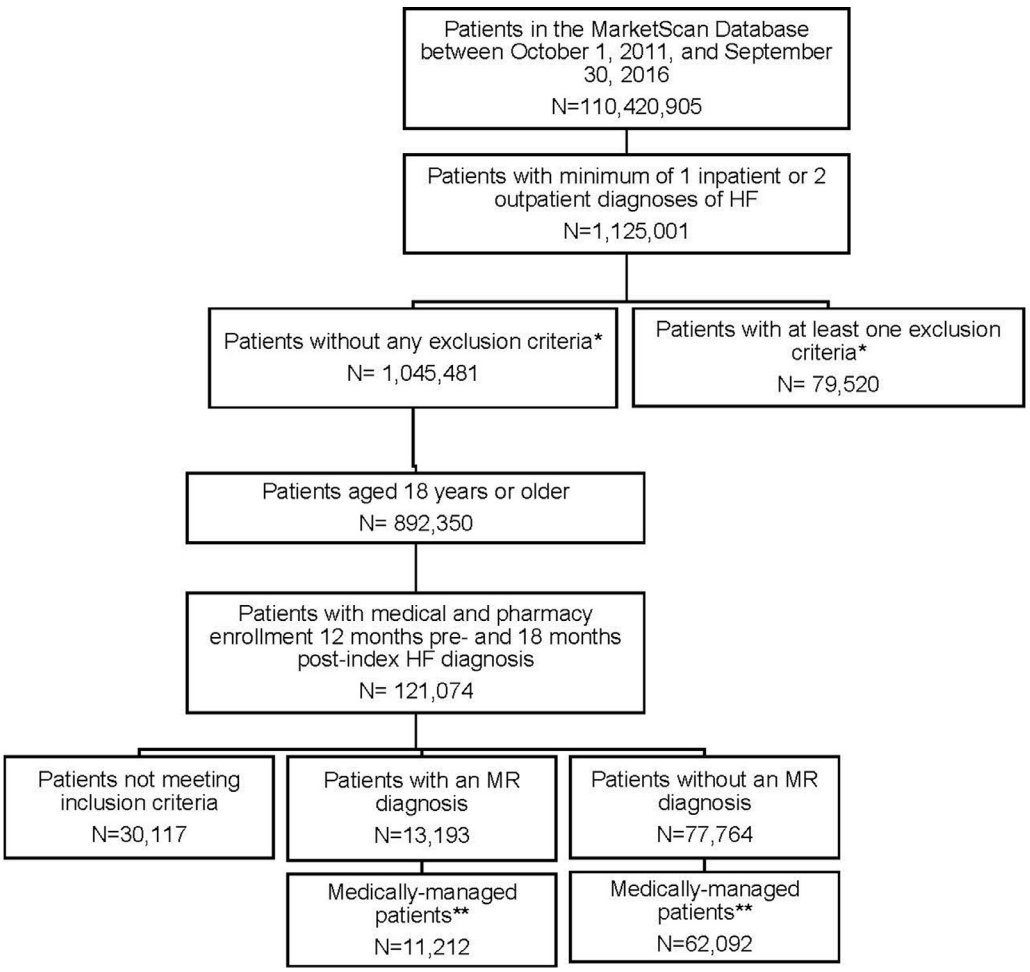


Figure 1. Attrition diagram. *Exclusion criteria include a record of ESRD anytime or a record of any of the following during the pre- or landmark-period: LVAD, heart transplant, chordal rupture, mitral stenosis, rheumatic mitral insufficiency, rheumatic tricuspid insufficiency, or hospice (palliative) care. **Medically managed patients were defined as patients with ≥2 HF medication fills 6 months to 18 months post-HF diagnosis. ESRD = end-stage renal disease; HF = heart failure; LVAD = left ventricular assist device.

All 3 cohorts were described by patient demographics, co-morbidities, and the intensity of medical management. Descriptive analytics were presented as mean and standard deviation for continuous variables or count and percentage for categorical variables. The Elixhauser Comorbidity Index (ECI)[16] was used to quantify patient baseline co-morbidities. The ECI is a validated set of 31 categories of co-morbidities that are associated with mortality. These co-morbidities were identified using diagnosis codes that appeared in the 12-month period before a patient's index diagnosis of HF (see Appendix E for complete code listing). In addition to the ECI, patients were identified for having ischemic heart disease (IHD). A patient was classified as having IHD with either a record of coronary artery disease, acute myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting before their diagnosis of HF (see Appendix F for coding detail).

Finally, a therapeutic intensity score was calculated based on patients' HF medication usage during the 12-month postperiod following the landmark period. The score is based on a previously published algorithm.[3] The medication categories and the cutoffs used in calculation of the score are included in Appendix G. Within each category, each prescription fill had 1 point assigned for low doses, 2 points for moderate doses, and 3 points for high doses. Points for each category (maximum of 3 from each) were summed for a total therapeutic intensity score (TIS) with the highest score of 24.

Multivariable models were generated to quantify the economic burden of MR in patients with HF on the outcomes of expenditures, total hospital days, and hospitalization for HF in the 12-month postperiod following the 6-month landmark period. Total expenditures by MR cohort were analyzed using a generalized linear model with a log link and an assumed underlying gamma distribution. The gamma distribution was chosen to account for the right-skewed nature of healthcare expenditures. The association of HF and MR was evaluated by analyzing total hospital days and hospitalizations for HF using a generalized linear model with a log link and an assumed underlying Poisson or negative binomial distribution. The Poisson or negative binomial distributions were chosen due to the discrete and positive nature of the count data (days and number of HF admissions). Separate models were estimated using this methodology: (1) total hospital days in the post period and (2) number of HF hospitalizations with and without MR.

For all 3 models, parameter estimates and 95% confidence intervals were calculated as measures of association strength and precision, respectively. Patient demographics including age, sex, region, and insurance type were used as covariates in the models, in addition to composite ECI scores (to represent the patient's co-morbidities), presence of IHD, and HF treatment intensity score. All statistical analyses in this study were performed using SAS software, version 9.4 (SAS Institute, Inc., Cary, North Carolina).

Results

Of the 110,420,905 patients in the MarketScan Database between October 1, 2011 and September 30, 2016, 1,125,001 patients (1.0%) met the inclusion criteria for incident HF. The requirements outlined in the methods section regarding age, confounding cardiomyopathies, and enrollment were used to further refine the HF cohort, resulting in a population of 121,074 patients (10.8%) who were further screened for MR. Patients with HF and no MR-diagnosis formed the largest cohort, with 64.2% (77,764 patients) of the eligible set. Next, additional enrollment and medication-fill requirements were applied, which reduced this group to 62,092 patients (51.3%). Patients with a diagnosis of MR in the landmark period who met these additional criteria (11,212 of 121,074 [9.3%]) were separated into 2 cohorts based on MR severity, leaving the final HF and MR cohorts of sMR (5,995 patients) and iMR (5,217 patients). See Figure 1 for attrition diagram.

Age, sex, region, and insurance type distributions of each MR cohort are given in Table 1. The mean (SD) age of the no MR cohort was 70.3 (13.8) years. The iMR cohort was younger (68.4 [14.1]) and the sMR cohort (72.7 [12.9])

Table 1
Patient demographics by cohort

Variable	Mitral regurgitation		
	None (N = 62,092)	Insignificant (N = 5,217)	Significant (N = 5,995)
Age, mean ± SD, years	70.3 ± 13.8	68.4 ± 14.1	72.7 ± 12.9
Men	32,923 (53.0%)	2,516 (48.2%)	3,255 (54.3%)
Region			
Northeast	12,360 (19.9%)	1,091 (20.9%)	1,375 (22.9%)
North central	21,570 (34.7%)	1,783 (34.2%)	2,133 (35.6%)
South	21,099 (34.0%)	1,893 (36.3%)	1,924 (32.1%)
West	6,836 (11.0%)	435 (8.3%)	530 (8.8%)
Unknown	227 (0.4%)	15 (0.3%)	33 (0.6%)
Insurance type			
Commercial	21,710 (35.0%)	2,069 (39.7%)	1,618 (27.0%)
Medicare supplemental	40,382 (65.0%)	3,148 (60.3%)	4,377 (73.0%)
Elixhauser comorbidity index* score, mean ± SD	4.8 ± 2.11	4.7 ± 2.04	5.3 ± 2.11
Coronary heart disease†	28,602 (45.0%)	2,864 (46.6%)	2,593 (48.3%)

* See Appendix E for additional patient comorbidities at baseline by cohort.

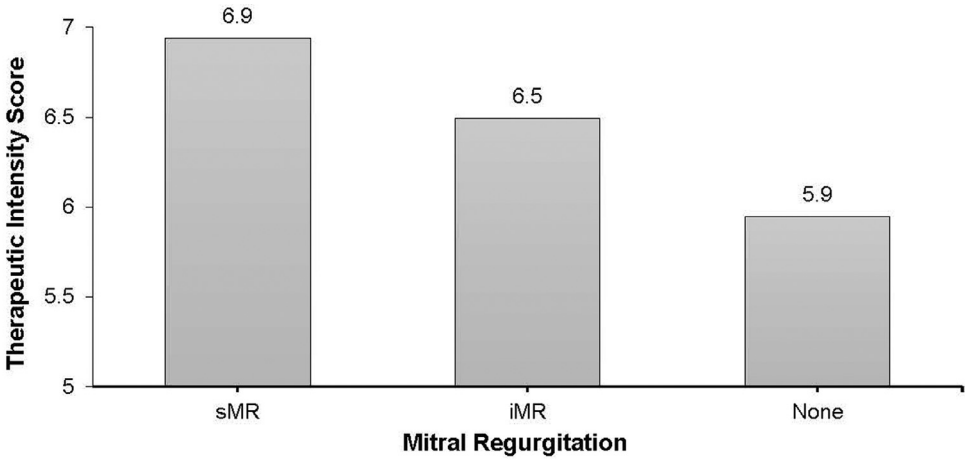
† Coronary Heart Disease was defined as a record of coronary artery disease, acute myocardial infarction, percutaneous coronary intervention, or coronary artery bypass graft before their Heart Failure diagnosis (see Appendix F for coding detail).

was older. Similarly, the sMR cohort had a higher frequency of Medicare Supplemental insurance in comparison to the other 2 cohorts. All cohorts had similar sex and regional distributions. The mean ECI scores varied by cohort, with the sMR cohort having the highest mean (SD) ECI score at 5.3 (2.11), followed by the no MR cohort at 4.8 (2.11) and the iMR cohort at 4.7 (2.04). Rates of IHD were higher in the sMR cohort (48.3%) followed by the iMR cohort (46.6%) and the no MR cohort (45.0%).

The mean TIS by MR cohort is shown in Figure 2. The sMR cohort had the highest TIS score with a mean of 6.9, followed by iMR at 6.5 and no MR at 5.9. Figure 3 displays therapeutic intensity and annualized healthcare expenditures. Of note, patients with a TIS score of zero did receive some attempt at medical therapy (based on inclusion) but did not have a medication refill record to qualify for a point on the TIS.

Total hospital days, expenditures (inpatient and outpatient), and HF hospital admissions were estimated for medically-managed patients with incident HF. Both unadjusted averages and model estimates are shown in Table 2. Overall, HF patients with MR had more total hospital days, higher expenditures, and an increased number of HF hospital admissions compared with HF patients without MR. All unadjusted averages were higher than estimated based on multivariable models, given that multivariable models consider differences in patient demographics, co-morbid conditions, and therapeutic intensity.

The sMR cohort had significantly more hospital days compared with the no MR cohort (least squares means estimates [LSME] of 1.91 vs 1.72 days; $p = 0.0096$). Total hospital days were not significantly different between the iMR cohort and the no MR cohorts (LSME 1.61 vs 1.72 days; $p = 0.1042$). The estimated annual expenditures in the sMR



Abbreviations: iMR, insignificant MR; MR, mitral regurgitation; sMR, clinically significant MR.

Figure 2. Therapeutic intensity score by MR cohort. MR = mitral regurgitation; iMR = nonclinically significant MR; sMR = clinically significant MR.

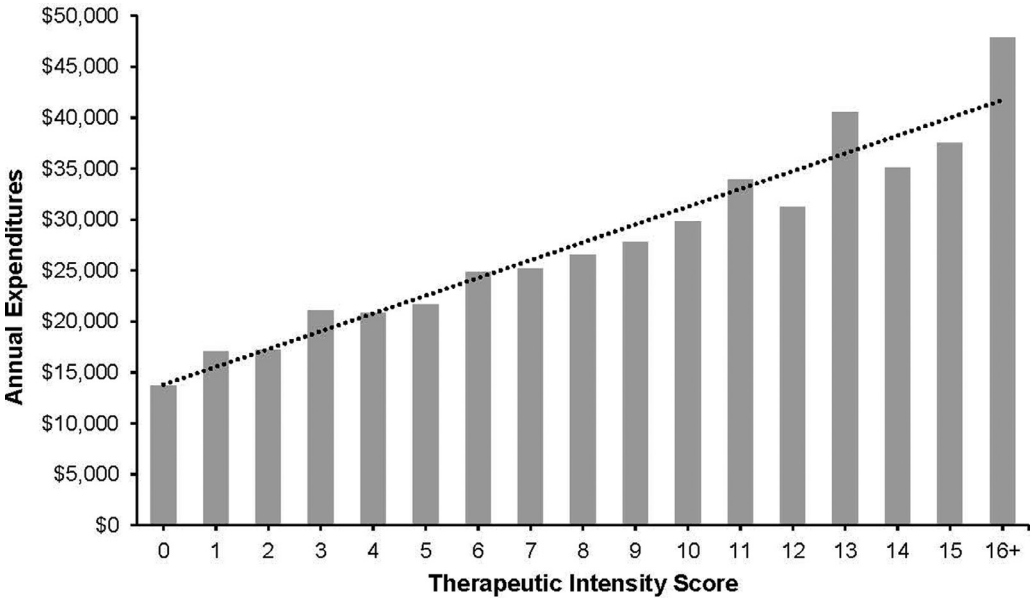


Figure 3. Therapeutic intensity score by annualized expenditures.

Table 2
Univariate and model estimates for all outcomes by cohort

Mitral regurgitation degree	Univariate estimates	Least squares means estimates*	p Value* (vs MR none)
Total annual hospital days (days)			
None	2.19	1.72	–
Insignificant	2.10	1.61	0.1042
Significant	2.86	1.91	0.0096
Total annual expenditures			
None	$23,837	$21,530	–
Insignificant	$24,756	$21,702	0.6728
Significant	$29,591	$23,988	<0.0001
Total annual HF admissions			
None	0.03	0.02	–
Insignificant	0.04	0.03	0.0064
Significant	0.07	0.04	<0.0001

MR = mitral regurgitation; CI = confidence interval; HF = heart failure.
* Based on multivariable models adjusted for patient demographics, comorbid conditions and therapeutic intensity.

cohort were significantly higher than the no MR cohort (LSME $23,988 vs $21,530; $p < 0.0001$). When evaluating total annual HF admissions, patients with sMR had an estimated 50% more admissions than the no MR cohort (LSME 0.036 vs 0.024; $p < 0.0001$). The iMR cohort also had 23% more HF hospital admissions in comparison to the no MR cohort (LSME 0.029 vs 0.024; $p = 0.0064$).

Discussion

In this retrospective, real-world analysis of medically-managed patients with an incident HF diagnosis, patients with concomitant sMR experienced significantly more HF admissions, hospital days, and annual expenditures. The increased utilization and expenditure results represent newly-diagnosed patients in their first year of medical management. The increase in expenditures comes from HF patients with sMR at the time of the HF diagnosis. Annually, patients with sMR have $2,400 more in healthcare expenditures, and 23% more HF hospital admissions in comparison to patients with no MR.

Few previous studies have examined the relation between secondary MR and HF in the first year of medically-managed patients with an incident HF-diagnosis. A 2017 study by Nasser et al[17] found that medical management (maximum tolerable doses of guideline-directed medical therapy [GDMT] for heart failure) could improve long-term prognosis and severity of secondary MR in a subset of patients with HF and reduced ejection fraction. This finding has implications for the usefulness of TIS when evaluating patients with both HF and MR, as therapeutic intensity could be used to track disease severity and patient prognosis.

The MITRA-FR trial[18] examined outcomes for patients with chronic HF and sMR but did not find a significant difference between percutaneous MV repair combined with medical therapy compared with medical therapy alone. In contrast, the COAPT trial,[19] which examined the effect of percutaneous MV repair in patients with HF and moderate-to-severe secondary MR, demonstrated percutaneous MV repair plus GDMT resulted in lower rates of HF hospitalizations and all-cause mortality at 24-month follow-up compared with GDMT alone. The contrasting results found in these trials are mainly attributed to different patient characteristics and selection criteria.[20] However, with further exploration of the right treatment for the right patient, these findings suggest novel treatment and techniques may help reduce hospitalizations that are anticipated with our data. Of note, cohorts from the COAPT and Mitra-FR trials evaluated chronic sMR patients, which differ from the present study of incident HF patients with concomitant MR.

Vemulapalli et al demonstrated percutaneous MV repair reduced Medicare costs 1 year after intervention compared with pre-MV repair.[21] Additionally, a 12-month retrospective, population-based analysis from a French National Payer documented 45% (€132.3 million) of the overall annual cost of MR in France was attributed to patients with MR and HF who were managed medically, as opposed to patients who underwent MV repair or replacement surgery.[22] The same study reported that medically-managed patients with MR and HF were associated with longer average hospital lengths of stay compared with both patients without HF and those who received surgery. The present study found similar high utilization rates and costs of HF patients with MR in this US-based claims analysis.

Our study has all the limitations of retrospective analyses using claims data. Although statistical modeling was used to control for potential confounding, models could not control for variables that were not included in the administrative database, including echocardiography results. We recognize that we relied upon proxies in automated data that suggested significant mitral regurgitation without having the quantitation of MR from imaging data. The expenditures, admissions, and hospital days reported do not include expenditures and hospital admissions which would have occurred in the landmark period. In conclusion, the presence of MR based on a retrospective claims database significantly increases the clinical and economic burden of medically-managed patients with incident HF. The rates of healthcare utilization and the associated financial burden are both more pronounced when MR is clinically significant.

Disclosures

PAM, HSM, CMB, DPC, and CG have consulting relations with Edwards Lifesciences. CMB is an advisory board member for Medtronic and Boston Scientific. DPC has a

consulting relation with Abbott Laboratories and participates in a speaker's bureau for Boston Scientific. HSM has a consulting relation with Abbott Laboratories, Boston Scientific and participates in a speaker's bureau for Actelion Pharmaceuticals, Bayer Healthcare Pharmaceuticals and Bristol-Myers Squibb Company. ERB and MPR are employees of CTI Clinical Trial & Consulting Services, which is a consultant to Edwards Lifesciences. JV, SM, and PV are employees of Edwards Lifesciences, the study sponsor.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.07.033.

1. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, Chiuve SE, Cushman M, Delling FN, Deo R, de Ferranti SD, Ferguson JF, Fornage M, Gillespie C, Isasi CR, Jimenez MC, Jordan LC, Judd SE, Lackland D, Lichtman JH, Lisabeth L, Liu S, Longenecker CT, Lutsey PL, Mackey JS, Matchar DB, Matsushita K, Mussolino ME, Nasir K, O'Flaherty M, Palaniappan LP, Pandey A, Pandey DK, Reeves MJ, Ritchey MD, Rodriguez CJ, Roth GA, Rosamond WD, Sampson UKA, Satou GM, Shah SH, Spartano NL, Tirschwell DL, Tsao CW, Voeks JH, Willey JZ, Wilkins JT, Wu JH, Alger HM, Wong SS, Muntner P, American Heart Association Council on E, Prevention Statistics C, Stroke Statistics S. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. *Circulation* 2018;137:e67–e492.
2. Braunschweig F, Cowie MR, Auricchio A. What are the costs of heart failure? *Europace* 2011;13(Suppl 2):ii13–ii17.
3. Vasudevan A, Munkres A, Shin H, Syed Abdul Sarmast S, McCullough P. Integration of cardiac biomarkers into a disease-specific score and its relation to intensity of medical therapy. *Heart Circ* 2017;1:5–9.
4. Agricola E, Ielasi A, Oppizzi M, Faggiano P, Ferri L, Calabrese A, Vizzardi E, Alfieri O, Margonato A. Long-term prognosis of medically treated patients with functional mitral regurgitation and left ventricular dysfunction. *Eur J Heart Fail* 2009;11:581–587.
5. De la Espriella R, Santas E, Minana G, Bodi V, Valero E, Paya R, Nunez E, Paya A, Chorro FJ, Bayes-Genis A, Sanchis J, Nunez J. Functional mitral regurgitation predicts short-term adverse events in patients with acute heart failure and reduced left ventricular ejection fraction. *Am J Cardiol* 2017;120:1344–1348.
6. Kajimoto K, Minami Y, Otsubo S, Sato N, investigators of the Acute Decompensated Heart Failure Syndromes r. Ischemic or nonischemic functional mitral regurgitation and outcomes in patients with acute decompensated heart failure with preserved or reduced ejection fraction. *Am J Cardiol* 2017;120:809–816.
7. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet* 2006;368:1005–1011.
8. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, de Ferranti SD, Floyd J, Fornage M, Gillespie C, Isasi CR, Jimenez MC, Jordan LC, Judd SE, Lackland D, Lichtman JH, Lisabeth L, Liu S, Longenecker CT, Mackey RH, Matsushita K, Mozaffarian D, Mussolino ME, Nasir K, Neumar RW, Palaniappan L, Pandey DK, Thiagarajan RR, Reeves MJ, Ritchey M, Rodriguez CJ, Roth GA, Rosamond WD, Sasson C, Towfighi A, Tsao CW, Turner MB, Virani SS, Voeks JH, Willey JZ, Wilkins JT, Wu JH, Alger HM, Wong SS, Muntner P, American Heart Association Statistics C, Stroke Statistics S. Heart disease and stroke statistics-2017 update: a report from the American Heart Association. *Circulation* 2017;135:e146–e603.
9. Nishimura RA, Vahanian A, Eleid MF, Mack MJ. Mitral valve disease−current management and future challenges. *Lancet* 2016;387:1324–1334.
10. Asgar AW, Mack MJ, Stone GW. Secondary mitral regurgitation in heart failure: pathophysiology, prognosis, and therapeutic considerations. *J Am Coll Cardiol* 2015;65:1231–1248.
11. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2017;135:e1159–e1195.
12. Hussaini A, Kar S. Percutaneous mitral valve repair: potential in heart failure management. *Curr Heart Fail Rep* 2010;7:22–26.
13. de Marchena E, Badiye A, Robalino G, Junttila J, Atapattu S, Nakamura M, De Canniere D, Salerno T. Respective prevalence of the different carpentier classes of mitral regurgitation: a stepping stone for future therapeutic research and development. *J Card Surg* 2011;26:385–392.
14. Danielson E. *Health Research Data for the Real World: The MarketScan® Databases*. Ann Arbor, MI: Truven Health Analytics Inc.; 2014.
15. McCullough PA, Philbin EF, Spertus JA, Kaatz S, Sandberg KR, Weaver WD, Resource Utilization Among Congestive Heart Failure S. Confirmation of a heart failure epidemic: findings from the Resource Utilization Among Congestive Heart Failure (REACH) study. *J Am Coll Cardiol* 2002;39:60–69.
16. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36:8–27.
17. Nasser R, Van Assche L, Vorlat A, Vermeulen T, Van Craenenbroeck E, Conraads V, Van der Meiren V, Shivalkar B, Van Herck P, Claeys MJ. Evolution of functional mitral regurgitation and prognosis in medically managed heart failure patients with reduced ejection fraction. *JACC Heart Fail* 2017;5:652–659.
18. Obadia JF, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, Lefevre T, Piot C, Rouleau F, Carrie D, Nejjari M, Ohlmann P, Leclercq F, Saint Etienne C, Teiger E, Leroux L, Karam N, Michel N, Gilard M, Donal E, Trochu JN, Cormier B, Armoiry X, Boutitie F, Maucort-Boulch D, Barnel C, Samson G, Guerin P, Vahanian A, Mewton N, Investigators M-F. Percutaneous repair or medical treatment for secondary mitral regurgitation. *N Engl J Med* 2018;379:2297–2306.
19. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, Whisenant B, Grayburn PA, Rinaldi M, Kapadia SR, Rajagopal V, Sarembock IJ, Brieke A, Marx SO, Cohen DJ, Weissman NJ, Mack MJ, Investigators C. Transcatheter mitral-valve repair in patients with heart failure. *N Engl J Med* 2018;379:2307–2318.
20. Atianzar K, Zhang M, Newhart Z, Gafoor S. Why did COAPT win while MITRA-FR failed? Defining the appropriate patient population for MitraClip. *Interv Cardiol* 2019;14:45–47.
21. Vemulapalli S, Lippmann SJ, Krucoff M, Hernandez AF, Curtis LH, Foster E, Qasim A, Wang A, Glower DD, Feldman T, Hammill BG. Cardiovascular events and hospital resource utilization pre- and post-transcatheter mitral valve repair in high-surgical risk patients. *Am Heart J* 2017;189:146–157.
22. Trochu JN, Le Tourneau T, Obadia JF, Caranhac G, Beresniak A. Economic burden of functional and organic mitral valve regurgitation. *Arch Cardiovasc Dis* 2015;108:88–96.