use in the United States is heterogeneous. Second, physicians tend to prescribe longer durations of $P2Y_{12}$ inhibitor in SIHD than currently recommended, especially with DES. This finding is particularly relevant given studies supporting DES use over BMS in patients at high bleeding risk. The ability to determine drug prescription patterns and adoption of findings from RCTs rely on an accurate mechanism to assess medication use. Our study highlights that over-the-counter aspirin limits the ability to examine DAPT using claims data. This is becoming increasingly germane in current era as more evidence mounts for reducing aspirin duration in PCI patients at high bleeding risk, including those not on an OAC.[4]

Disclosures

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Trends of Co-morbidities in Clinical Trials of Lipid Lowering Therapies

Dyslipidemia is an established risk factor for cardiovascular disease.[1] Although optimal management of dyslipidemia can reduce cardiovascular risk burden,[2] a significant proportion of patients with dyslipidemia carry significant co-morbidity burden, influencing the quality of life, and outcomes.[1] Hence, it is imperative that randomized controlled trials examining the efficacy of lipid-lowering therapy should recruit patients reflective of the real-world multimorbid population. Accordingly, we systematically reviewed the prevalence and temporal changes in comorbidities reported in lipid-lowering therapy trials to gain further insights on this issue.[3]

A total of 61 randomized controlled trials (n = 485,678) with follow-up of ≥3 months were identified using MEDLINE and Clinicaltrials.gov (January 1993-December 2018).[4] Categorical variables were reported as No. (%) and were compared using Chi-square testing. Trends of co-morbidities were tested using simple linear regression model using the publication year as an independent variable. SPSS V-24 (IBM Corporation) was used for all analyses.

The median number of participants per trial was 5,011 (IQI, 2,805 to 10,944). Mean age ± SD was 62.4 ± 4.33 years with 31.7% of participants being females. 33 trials used statins, 3 trials used ezetimibe, 6 trials used PCSK9 inhibitors, 5 trials fibrates, 2 niacin trials, and 12 trials used omega 3 fatty acids. A total of 47.5% were primary prevention trials and 52.5% were secondary prevention trials. Diabetes mellitus was reported by 86.9% of trials, hypertension 73.6%, stroke 42.6%, coronary artery disease (CAD) 42.6%, and peripheral artery disease (PAD) by 39.3% of trials. A total of 83.6% reported smoking status while body mass index was reported by 55.7% trials. Only 3.3% trials reported chronic kidney disease (CKD) and cancer or chronic obstructive pulmonary disease (COPD) were reported by only 6.6% of trials, each. The prevalence of CAD (from 57.1% in 1993-1998 to 30.9% in 2014-2018) and PAD (from 11.6 % in 1999-2003 to 4.2 % in 2014-2018) decreased, and enrollment of hypertensives (from 23.8% in 1993-1998 to 59.2% in 2014-2018), diabetics (6.2% in 1993-1998 to 35.8% in 2014-2018), and patients with cerebrovascular accident (CVA) (from 2.1% in 1993-1998 to 7.2% in 2014-2018) increased (Table 1). Enrollment of patients with CKD, COPD and cancer remained consistently low. Compared with primary prevention trials, enrollment of active smokers (21.3% vs 13.9%) and hypertensives (54.1% vs 43.6%) was higher in secondary prevention trials, whereas, diabetics (30.9% vs 26.9%) were more prevalent in primary versus secondary prevention trials.

Between 1993 and 2018, the enrollment of patients with cardiovascular and noncardiovascular comorbidities varied over time in trials of lipid-lowering therapy. The prevalence of cardiovascular risk factors, such as smoking or hypertension, and of non-cardiovascular diseases such as CKD, COPD, and cancer remained consistently low. Interestingly, the enrollment of patients with CAD and PAD also declined over the years in trials

Table 1
Trends in comorbidities in clinical trials of lipid lowering therapies

Year	1993−1998 (Population = 33,230, trials=7)		1999−2003 (Population = 78,249, trials =13)		2004−2008 (Population = 113,731, trials =17)		2009−2013 (Population = 69,538, trials =11)		2014−2018 (Population = 190,930, trials= 13)	
Comorbidities	Trials, No (%)	Patients with Comorbidity, No (%)	Trials, No (%)	Patients with Comorbidity, No (%)	Trials, No (%)	Patients with Comorbidity, No (%)	Trials, No (%)	Patients with Comorbidity, No (%)	Trials, No (%)	Patients with Comorbidity, No (%)
Current smoker	7 (100.0)	7,060 (21.2)	11 (84.6)	18,365 (23.5)	12 (70.6)	13,200 (11.6)	10 (90.9)	10,727 (15.4)	11 (84.6)	37,454 (19.6)
Former smoker	3 (42.9)	10,188 (30.7)	5 (38.5)	20,862 (26.7)	7 (41.2)	20,637 (18.1)	4 (36.4)	12,002 (17.3)	2 (15.4)	19,388 (10.2)
Coronary artery disease	4 (57.1)	18,968 (57.1)	8 (61.5)	40,965 (52.4)	6 (35.3)	26,001 (22.9)	3 (27.3)	18,006 (25.9)	5 (38.5)	59,078 (30.9)
Diabetes mellitus	5 (71.4)	2,055 (6.2)	12 (92.3)	17,626 (22.5)	15 (88.2)	31,314 (27.5)	8 (72.7)	20,308 (29.2)	13 (100.0)	68,265 (35.8)
Hypertension	5 (71.4)	7,897 (23.8)	12 (92.3)	45,304 (57.9)	12 (70.6)	38,875 (34.2)	6 (54.5)	34,030 (48.9)	10 (76.9)	112,978 (59.2)
Chronic kidney disease	–	–	1 (7.7)	2,102 (2.7)	–	–	1 (9.1)	9,270 (13.3)	–	–
Heart failure	1 (14.3)	166 (0.5)	3 (23.1)	573 (0.7)	8 (47.1)	18,913 (16.6)	2 (18.2)	690 (1.0)	3 (23.1)	2,368 (1.2)
Stroke	1 (14.3)	701 (2.1)	7 (53.8)	5,481 (7.0)	9 (52.9)	76,64 (6.7)	5 (45.5)	3,528 (5.1)	4 (30.8)	13,836 (7.2)
Peripheral vascular disease	–	–	7 (53.8)	9,062 (11.6)	9 (52.9)	4,485 (3.9)	4 (36.4)	2,111 (3.0)	4 (30.8)	7,996 (4.2)
Cancer	–	–	–	–	3 (17.6)	605 (0.5)	1 (9.1)	553 (0.8)	–	–
COPD	–	–	1 (7.7)	88 (0.1)	2 (11.8)	2,593 (2.3)	1 (9.1)	230 (0.3)	–	–
Body mass index (kg/m^2)	2 (28.6)	–	6 (46.2)	–	11 (64.7)	–	7 (63.6)	–	8 (61.5)	–

of lipid-lowering therapies. These results call for review of entry criteria for clinical trials that would more accurately reflect the multimorbid real-world population using lipid-lowering therapy. The limitations of our study include lack of access to patient-level data, limited reporting of co-morbidities, a potential reporting and selection bias, and lack of assessment of geographical variation, funding sources, and racial demographics and their influence on co-morbidity burden. In *conclusion*, reporting of comorbid conditions in lipid lowering therapy trials remained consistently low and varied over 3 decades. These findings highlight entry bias in clinical trials and demand innovative strategies to accommodate the participants reflecting the real-world population with multimorbidity burden.

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