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Characteristics of patients with dyslipidemia treated in routine care setting in China

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ABSTRACT

Objective: To describe characteristics of patients with dyslipidemia treated in routine care in China overall and stratified by diabetes and atherosclerotic cardiovascular disease (ASCVD).

Methods: This study used data from a cross-sectional survey conducted in China in 2017 under the Dyslipidemia Disease Specific Programme (DSP). Each surveyed physician provided information including demographics, dyslipidemia diagnosis and treatment history, lab values on at least 8 patients currently treated for dyslipidemia with oversampling of patients with ASCVD or diabetes mellitus diagnosis at the time of survey. A related patient survey assessed treatment adherence and satisfaction.

Results: This study included 195 physicians (40 endocrinologists, 75 internists, 80 cardiologists) who provided data on 1870 patients (852 with diabetes; 1018 patients without diabetes). Among patients with diabetes, 279 had ASCVD and 573 did not (non-ASCVD). In the diabetic population, patients with ASCVD were older (67.3 vs. 62.1 years), more often had caregiver support (34 vs. 14%), and had higher average LDL-C at diagnosis (172.4 vs. 167.4 mg/dL) compared to their non-ASCVD counterparts. Findings were similar for non-diabetic patients (ASCVD: 323 patients; non-ASCVD: 695) patients. In all four subgroups, 46–54% of patients reported low treatment adherence, and fewer than half expressed satisfaction with their cholesterol control, and 2–5% had LDL-C < 70 mg/dL at their most recent assessment.

Conclusions: Among patients with dyslipidemia, those with ASCVD had higher LDL-C levels than patients without ASCVD, and many required caregiving. Low levels of treatment adherence, LDL-C control, and patient satisfaction suggest opportunities to improve care for Chinese patients with dyslipidemia.

Introduction

During the recent multi-decade period of rapid economic expansion and social change in China¹, important demographic and lifestyle shifts have occurred, and the burden of cardiovascular disease has grown. The proportion of the population aged 65 years and older will increase from 10% in 2014 to 17% in 2030; this is a faster rate of increase than currently exhibited in any other country in the world^{1,2}. In addition to the aging of the population, dietary changes marked by increased meat consumption and decreased intake of vegetables and grains, along with the adoption of a more sedentary lifestyle overall, coincide with increasing prevalence of cardiovascular diseases (CVD) and associated risk factors (e.g. dyslipidemia, diabetes mellitus) among Chinese adults over time¹.

CVD has been the leading cause of death in China since the late 1980s, and as of 2014 CVD accounted for over 40% of all deaths in both urban and rural populations in this country³. Stroke is of particular importance and is currently the leading cause of death among both men and women³. The current prevalence of CVD-related mortality reflects substantial increases from 1990 to 2013, an interval in which the number of CVD-related deaths, ischemic heart disease deaths and stroke deaths increased by 46, 91, and 48%, respectively³. An ongoing trend of increasing prevalence of known risk factors for atherosclerotic cardiovascular disease (ASCVD) including hypertension, dyslipidemia, obesity, and diabetes, coincides with these mortality trends¹.

In general, the literature shows that dyslipidemia is an important contributor to the risk of ASCVD and related mortality in the general population, and the lipid abnormalities associated with type 2 diabetes also play a major role in the excess ASCVD risk observed among individuals with diabetes⁴. Although CVD risk profiles (e.g. demographics, lifestyles, clinical characteristics) are rapidly changing among adults in China, international literature offers a very incomplete picture of Chinese patients who are receiving treatment for dyslipidemia. Therefore, the current study was undertaken to describe the characteristics and clinical profiles of these patients, and to describe characteristics of

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important subgroups in this patient population (i.e. patients with/without diabetes mellitus and with/without ASCVD).

Methods

Data source and survey respondents

This study used data from a cross-sectional survey conducted in China in 2017, under the Adelphi Dyslipidemia Disease Specific Programme (DSP)^{5,6}. In this DSP, a geographically representative sample of physicians (internists, cardiologists, and endocrinologists) was identified and screened for eligibility to participate in the survey. The sample was drawn from among physicians prescribing lipid-lowering therapies in 14 cities across the country (Beijing, Shanghai, Guangzhou, Shengyang, Nanjing, Chengdu, Wuhan, Chongging, Tianjing, Hangzhou, Xi'an, Zhengzhou, Dalian, and Qingdao), and the distribution across specialty types reflects feasibility considerations and a desire to include a robust number of each type of physician. To be included in the DSP, physicians were required to be treating at least 10 patients with diagnosed dyslipidemia per typical week and to be responsible for the lipid management treatment decisions for these patients. Participating physicians were consented into the study and compensated at fair market research rates consistent with the time required to complete study-related activities.

Each surveyed physician provided diagnoses using a precoded checklist, full treatment history, laboratory values, and other relevant characteristics for at least eight consecutive consulting patients who were being actively treated with lipid-lowering therapy (LLT) for dyslipidemia and met inclusion criteria at the time of the survey. This approach provides a pseudo-random sample of patients as no other selection criteria are applied. Physicians reported data on whether or not each patient carried a diabetes diagnosis (type 1 or type 2) and whether or not each patient met diagnostic criteria for ASCVD (defined below). These data were, in turn, used to classify patients for stratified analyses. In addition to these eight patients which represent a sample of each physician's general dyslipidemia consulting practice, physicians were also invited to contribute data for up to two additional patients who carried a diagnosis of ASCVD at the time of the survey. This oversampling was performed to enhance the number of ASCVD patients included in the study in an effort to help ensure a sufficient sample for the planned stratified analyses. For this study, ASCVD was defined by the presence of diagnoses for any of the conditions: acute coronary syndrome (ST-elevation myocardial infarction [STEMI], non-STEMI [NSTEMI], unstable angina); stroke or transient ischemic attack; stable angina; history of an interventional cardiac procedure (percutaneous coronary intervention [PCI], coronary artery bypass grafting [CABG]); peripheral arterial disease (PAD). In order to enhance the sample of diabetic patients included in the study, a separate sample of 40 endocrinologists was recruited; these physicians each provided data for eight additional diabetic patients on LLT and seen consecutively in their clinics.

Patients for whom physicians reported data were invited to voluntarily complete a questionnaire, independently of their physician, to report their attitudes about their condition, treatment adherence (Morisky Medication Adherence Scale [MMAS-8]) and satisfaction. Scores on the Morisky Scale were grouped to define low (<6 points), medium (6 to <8 points), and high (8 points) adherence. Using a checkbox, all recruited patients provided informed consent for use of their anonymized self-reported data and to allow publication of aggregated data in scientific journals. Data were collected in such a way that patients and physicians could not be identified directly; responses were not shared between the two types of respondents, and all data were aggregated and deidentified before receipt.

DSP data were collected in accordance with Adelphi Real World procedures, which are compliant with the Health Information Technology for Economic and Clinical Health (HITECH) Act, the Health Insurance Portability and Accountability Act (HIPAA), and all applicable local laws regarding research subject privacy. This research also obtained ethics approval from the Freiburg Ethics Commission International (FEKI). For the current study, logic checks were conducted to ensure that numerical values for key variables were within an appropriate range. For individual analyses, only cases with complete data for the required variables were included.

For each patient, the treating physician reported data on age, sex, ethnicity, employment status, and use of caregiver were collected for each patient. Body mass index (kg/m^2) was calculated from the height and weight physicians reported for each patient, and values were grouped into five categories based on categories recommended by the World Health Organization⁷. Physicians also reported patientspecific data on the type of hyperlipidemia diagnosis and time since diagnosis, comorbidities including the history of acute coronary syndrome events, a physician-defined LDL-C target for each patient, laboratory test history over last 12 months, and results of key lipid assessments during that time period. Physicians and patients also both reported whether or not they were satisfied with the most recent lipid test results. Current and previous LLT was characterized by drug class and agent. In addition, medication dose was reported for currently used lipid-lowering agent(s).

Statistical analysis

Analyses were primarily descriptive in nature. Continuous variables were summarized using mean and standard deviations (SD), and categorical variables were summarized using frequency and percentages. Results are reported for patients overall and also stratified by the presence of ASCVD and/or diabetes mellitus. Those patients with ASCVD and/or diabetes mellitus were defined as high risk for the purpose of analysis. Significance testing was performed for pairwise comparisons with Fisher's exact test used for comparisons with two response categories and chi-squared tests used for comparisons with more than two response categories. Mann–Whitney tests were used for comparisons involving ordinal categorical responses (e.g. adherence) and *t*-tests were used for comparisons involving numerical variables.

Results

Patient demographic and clinical characteristics

This study included 195 physicians (40 endocrinologists, 75 internists, 80 cardiologists) who provided data on 1870 patients of whom 852 had been diagnosed with diabetes by the time of the survey. All patients completed the patient survey. Characteristics of study patients at diagnosis are provided in Table 1. Compared with non-diabetic patients (n =-1,018), individuals with diabetes (n = 852) were older on average (p < 0.0001) and a greater percentage of diabetic patients were retired or had a caregiver (p < .0001, p < .005, respectively). Among diabetic patients, 47% had been diagnosed with combined hyperlipidemia (hypercholesterolemia/ hypertriglyceridemia) compared with 39% of patients without diabetes (p < .001). This finding was reversed for the diagnosis of hypercholesterolemia alone (p < .0050). Similar percentages of patients with and without diabetes carried a diagnosis of hypertriglyceridemia and familial combined hyperlipidemia (p > .6).

Approximately one-third of patients with (279/852) and without diabetes (323/1018) had been diagnosed with ASCVD, and results stratified by both diabetes and ASCVD status are provided in Tables 1 and 2, and Figure 1. Patients with both diabetes and ASCVD were more frequently diagnosed with combined hyperlipidemia than patients in any

Table 1. Patient demographics and dyslipidemia at diagnosis.

other subgroup (Figure 1). Among patients with diabetes, those individuals who also had ASCVD were older on average (67.4 vs. 62.2 years, p < .0001) and 34% of these dually-diagnosed patients reported having caregiver support compared with 14% of their counterparts with diabetes who did not have ASCVD (p < .0001, Table 1).

In addition, patients with both diabetes and ASCVD had more comorbidities on average than any other group. These dually-diagnosed patients were also more likely to have retinopathy and neuropathy, which are both adverse events of special interest in the diabetic population, than were patients in any other subgroup. The time since hyperlipidemia diagnosis was longer among patients with both diabetes and ASCVD than among those without ASCVD (p < .0001). The dually-diagnosed patients also had a numerically higher average LDL-C at the time of their hyperlipidemia diagnosis compared to their diabetic counterparts who did not have ASCVD although this difference was not statistically significant (172.4 vs. 167.4 mg/dL, p = .07).

Similar patterns were observed among non-diabetic patients (Tables 1 and 2, Figure 1). In the non-diabetic population, the diagnosis of combined hyperlipidemia was more common (p < 0.002) among those who had also been diagnosed with ASCVD (n = 323) than their non-ASCVD counterparts (n = 695) and on average, more time had elapsed since their hyperlipidemia was diagnosed (p < .0001).

		With diabete	25					
Characteristic	All n = 852	With ASCVD $n = 279$	Without ASCVD $n = 573$	<i>p</i> -Value	All n = 1018	With ASCVD $n = 323$	Without ASCVD n=695	<i>p</i> -Value
Age (years) [mean (SD)]	63.8 (10.4)	67.4 (9.6)	62.2 (10.3)	<.0001	61.6 (11.5)	66.1 (10.3)	59.5 (11.4)	<.0001
Male (%)	57	59	56	.34	59	63	57	.06
Employment status (%)								
Working full time	19	11	23	<.0001	28	16	33	<.0001
Working part time	1	1	2	.76	2	3	2	.33
Homemaker	6	4	7	.81	7	5	8	.18
Student	0	0	0	NA	<1	0	<1	1
Retired	72	83	66	<.0001	62	74	56	<.0001
Unemployed	2	2	2	.80	1	2	1	.56
Has caregiver (%)	21	34	14	<.0001	15	29	9	<.0001
Time since diagnosis (years) [mean (SD)]	2.4 (2.7)	3.4 (3.5)	2.0 (2.1)	<.0001	1.9 (2.5)	2.6 (2.8)	1.6 (2.3)	<.0001
LDL-C at diagnosis (mg/dL) [mean (SD)]	168.9 (33.0)	172.4 (33.8)	167.4 (32.6)	.07	168.4 (34.86)	171.7 (37.1)	167.1 (33.9)	.08
Statin use	88	94	85	.002	89	95	86	<.0001

ASCVD atherosclerotic cardiovascular disease; NA, not applicable.

Table 2. Patient comorbidities.

	With diabetes				Without diabetes			
Characteristic	All n = 852	With ASCVD $n = 279$	Without ASCVD $n = 573$	<i>p</i> -Value	All n = 1018	With ASCVD $n = 323$	Without ASCVD n = 695	<i>p</i> -Value
Number of comorbidities [mean (SD)] ^a	3.0 (1.9)	4.4 (2.1)	2.2 (1.3)	<.0001	2.8 (1.6)	4.1 (1.5)	2.2 (1.3)	<.0001
Comorbidities (%) (\geq 15% frequency in any group)								
Hypertension	74	81	70	.0004	77	80	76	.3
Atherosclerosis	37	59	26	<.0001	33	54	23	<.0001
Coronary heart/artery disease	34	56	23	<.0001	38	62	27	<.0001
Unstable angina	13	36	2	<.0001	15	42	3	<.0001
Peripheral vascular disease	7	20	0	<.0001	3	9	0	<.0001
Myocardial infarction	7	18	2	<.0001	6	14	2	<.0001
Stable angina	5	15	0	<.0001	5	16	0	<.0001
Comorbidities of special interest (%)								
Retinopathy	6	10	4	.0007	1	1	1	.77
Neuropathy	3	6	2	.0009	1	2	1	.15

ASCVD, atherosclerotic cardiovascular disease. ^aExcluding diabetes mellitus and dyslipidemia.





Approximately 29% of non-diabetics with ASCVD had a caregiver, compared with 9% of patients with neither diabetes nor ASCVD (p < 0.0001). The average ages for non-diabetics with and without ASCVD were 66.1 and 59.5 years (p < .0001), and the mean number of comorbidities were 4.1 and 2.2, respectively (p < .0001). The average LDL-C level at the time of hyperlipidemia diagnosis was 171.7 mg/dL among non-diabetics with ASCVD, and 167.1 mg/dL among non-diabetics without ASCVD (p = .08). At their most recent laboratory assessment, only a small percentage of patients in each subgroup had LDL-C < 70 mg/dL (diabetic patients: ASCVD: 5%, no ASCVD: 4%; non-diabetic patients: ASCVD: 5%, no ASCVD: 2%).

Lipid-lowering treatment patterns, adherence, and satisfaction

The majority (88%) of diabetic patients were using statins as their current LLT. Among those with both diabetes and ASCVD 94% were on statin therapy compared with 85% among patients with diabetes but without ASCVD (p < .0001). Atorvastatin and rosuvastatin, the most commonly used statins, were used by 51% and 19% of all diabetic patients. The mean (SD) daily doses reported for these agents were 20.1 (9.1) mg and 11.4 (3.8) mg. Among diabetics with ASCVD, 54% used atorvastatin and 25% used rosuvastatin while among diabetics without ASCVD, the corresponding proportions were 49 and 15%, respectively. Among non-diabetics with ASCVD, 50% used atorvastatin and 26% used rosuvastatin while among non-diabetics without ASCVD, the corresponding proportions were 46 and 16%, respectively. In both the diabetic and non-diabetic populations only the differences in the percentage of patients using rosuvastatin were statistically significant (p < .0005).

The overall distribution of patients by adherence level was not significantly different between diabetic patients with and without ASCVD (p = .5186). Among diabetic patients, 50% of those with ASCVD (total n = 276)) and 47% of those without ASCVD patients (total n = 570) reported low adherence to LLT (Figure 2). Among non-diabetic patients, however, adherence was significantly different between patients with and without ASCVD (p = .0217). The percentage of non-diabetic patients reporting low adherence to LLT was 54% for those with ASCVD and 46% for those without ASCVD. High adherence was reported by 23% of diabetics with ASCVD, 24% of diabetics without ASCVD, and the corresponding percentages among the non-diabetic patients were 20 and 25%, respectively.

Among diabetic patients, 42% of those with ASCVD patients and 49% of those without ASCVD patients reported that they were satisfied with their current level of cholesterol control. Among non-diabetic patients, 48% of ASCVD and 46% of non-ASCVD patients were similarly satisfied. Among diabetic patients who expressed dissatisfaction, 26% (non-ASCVD) to 30% (ASCVD) of patients believed better control could be achieved. Findings were reversed among the non-diabetic patients with regard to ASCVD status. Among non-diabetic patients who had expressed dissatisfaction with therapy, 24% of those ASCVD and 29% of those without ASCVD believed better control could be achieved.

The percentage of diabetic patients who reported "fully understanding" the need to take their medications increased from 14% among patients with low adherence to 22% among patients with high adherence. The patterns were similar among non-diabetic patients in whom the percentage who reported "fully understanding" the need to take their medications was 11% among those with low adherence and 24% among those with high adherence. In both the diabetic and non-diabetic populations, the percentage of patients



Figure 2. Self-reported adherence¹ to lipid-lowering therapies, stratified by diabetes and ASCVD status.

who reported being satisfied with their cholesterol levels increased from 44% among patients with low adherence to 52% among patients with high adherence.

Discussion

This study was undertaken to describe the characteristics, disease burden, treatment adherence and satisfaction of Chinese patients receiving LLT for dyslipidemia. Given that diabetes is associated with dyslipidemia and that both are important risk factors for ASCVD, results were stratified to characterize patients on lipid-lowering therapies according to the presence or absence of diabetes, and within those two subpopulations to provide insights for patients with and without diagnosed ASCVD. To our knowledge, this is the first study to include patient-reported data in addition to physician-reported data.

The results of this study suggest that there may be differences in how dyslipidemia manifests in patients with and without diabetes. Specifically, combination hyperlipidemia (hyperlipidemia along with hypertriglyceridemia) was diagnosed in nearly half of all diabetic patients, but in less than 40% of non-diabetic patients. By contrast, hypercholesterolemia alone was more common among patients without diabetes than among those with diabetes (45 vs. 39%). This finding suggests that dyslipidemia may present as a more complicated condition among patients who also have diabetes.

On the whole, the results from this study also suggest that patients on lipid-lowering therapy who have both diabetes and ASCVD are likely more clinically complex than any of the other types of patients studied. The overall disease burden as measured by the mean number of comorbidities (excluding dyslipidemia and diabetes) appears to be similar between patients with and without diabetes. However, dyslipidemia patients with both diabetes and ASCVD had a greater number of comorbidities, on average, than either other diabetic patients or non-diabetic patients, including those with ASCVD. Diabetics with ASCVD also exhibited specific indicators of greater CV-related disease burden, including retinopathy and neuropathy, than patients in any other subgroup studied. This hypothesis that study patients with both diabetes and ASCVD are likely to be medically fragile is also borne out by data on use of caregivers obtained in this study. Although a higher percentage of ASCVD patients, in general, required a caregiver compared with patients who did not have diagnosed ASCVD, the percentage of diabetic patients with ASCVD using caregivers was larger than for their non-diabetic counterparts.

While it was beyond the scope of the current study to formally assess relationships between treatment adherence, cholesterol control, and treatment satisfaction, we note that treatment adherence was generally low with as many as 50% of patients in any subgroup reporting low adherence, a minority of patients had LDL-C < 70 mg/dL at their most recent assessment and fewer than half of patients in all four subgroups studied reported satisfaction with the cholesterol control they had achieved on their current lipid-lowering therapies. In the full study population, patients classified as having high adherence were more likely to report understanding the need to take their medication and to report being more satisfied with their cholesterol levels, compared with patients classified as having low adherence. Despite dissatisfaction with their cholesterol control on current therapies, between one-quarter to one-third of patients expressed optimism that better control could be achieved. Real-world adherence with lipid-lowering therapies in China is not wellunderstood, however, a medical records/interview study of patients who initiated lipid-lowering drugs between 1 January 2004 and 28 February 2006 reported that the proportion of patients with good compliance (defined as medication possession ratio [MPR] ≥ 80%) ranged from 81% at 1 year to 57% at 3 years⁸. It is challenging to compare these results with the patient-reported data from our study since the data sources differ and the time since treatment initiation varies for the patients in our study. A recent systematic review examined adherence with statins (the current standard of care in China)⁹. Studies included in that review examined adherence over 6 months to 3 years with most evaluating a 2-year period. In studies that evaluated MPR as a dichotomous variable, the reported percentage of patients achieving MPR \geq 80% ranged from 18.3–91.9%; mean MPR values from studies that examined MPR as a continuous variable ranged from 0.28 to 1.

Our study provides a more detailed picture of the types of patients treated for dyslipidemia in routine practice in China. This greater understanding of such patients is important given the accumulating literature which highlights a rapidly growing burden of cardiovascular disease in China, as key risk factors for CVD and cardiovascular events becoming increasingly common among adults. Temporal changes in the incidence and prevalence of dyslipidemia and diabetes, which is itself associated with lipid abnormalities, exemplify these trends. The prevalence of high total cholesterol (>200 mg/dL) has been increasing since at least the early 1980s and dyslipidemia is estimated to be present in 34% of all Chinese adults age 18 years, 42% of men, and 33% of women, with a greater prevalence in urban areas (35%) than in rural areas (26%)¹. The prevalence of elevated LDL-C which was estimated at 6.5% in Chinese adults (age \geq 20 years) in 2008 was recently estimated at 7.96%)^{10,11}. Cross-sectional data from the China National Diabetes and Metabolic Disorders Study of adults age 20 years and older indicates that the 2007-2008 prevalence of diabetes was 11% in men and 9% in women, which represents a 300% increase since the 1994 national survey^{10,12,13}. Furthermore, data from a representative sample of patients age 40-70 years with type 2 diabetes treated at top-ranked endocrinology clinics across China indicates that 67% of these diabetic patients had dyslipidemia, and 8.5% had high low-density lipoprotein cholesterol levels $(\geq 4.14 \text{ mmol/L})^{14}$.

The mean age of diabetic patients in our study falls within the range of mean age reported in the International Diabetes Foundation's Executive Summary on diabetes and cardiovascular disease which indicates a CVD prevalence of 14.8–40.5% among individuals with mean age of 56–66 years in high- and middle-income countries. The age distribution in our study is also consistent with data for the United States, mean ages of 56.2 years and 66.5 years have been observed for Type 2 diabetics with and without ASCVD, although the percentage of the population comprised by males is higher than the approximate 50% reported in the United States.

Data on the use of lipid-lowering therapies is limited, but Pan et al reported a treatment prevalence of 19.5% among Chinese adults with dyslipidemia between 2007 and 2010, and a control rate of 8.9% defined by total cholesterol <240 mg/dL, and/or low density lipoprotein <160 mg/dL, and/or high density lipoprotein >40 mg/dL, and/or triglyceride <200 mg/dL)¹⁰. Among individuals with type 2 diabetes and dyslipidemia, Yan et al. found that only 56% received treatment, and 39% achieved LDL-C control (LDL-C < 2.60 mmol/L in general, <1.80 mmol/L in patients with an overt cardiovascular disease)¹⁴.

These previous assessments of the prevalence and treatment of dyslipidemia in China underscore the importance of planning for the projected burden of cardiovascular disease as China's population ages and its economy continues to transform^{15,16}. As CVD risk factors become more common, between 2016 and 2030, the incidence of acute myocardial infarctions (AMIs) is estimated to increase by 75 million and strokes by 118 million, while the total number of CVD deaths is expected to increase by 39 million¹⁵. Stevens et al suggest that universal treatment of appropriate patients with lipid and blood pressure-lowering therapies would be expected to avert between 10 and 20 million AMIs, 8 to 30 million strokes, and 3 to 10 million CVD deaths during this time period¹⁵. Along with this clinical and human impact, such a level of treatment is projected to concurrently produce a positive social value (after health care costs) as high as \$932 billion.

The results of our study indicate that among individuals who are receiving lipid-lowering therapies for dyslipidemia, those with both diabetes and ASCVD carry a particular burden. Our study also suggests opportunities for improving care for dyslipidemia patients in general. The majority of patients not only expressed dissatisfaction with their lipid-lowering treatments but also reported having been unable to achieve good adherence to treatment, and a minority of patients at high risk had achieved LDL-C of <70 mg/dL at their most recent laboratory assessment. This study provides a more detailed picture of patients receiving lipid-lowering therapies in China than previously available, and our results suggest that there may be opportunities to improve clinical outcomes as well as treatment adherence and satisfaction in this population.

Note

1. Morisky Scale. Use of the MMAS is protected by US copyright and registered trademark laws. Permission for use is required. A license agreement is available from Donald E. Morisky, 294 Lindura Court, Las Vegas, NV 89138-4632. dmorisky@gmail.com

Transparency

Declaration of funding

Amgen Inc. sponsored this study.

Declaration of financial/other relationships

GL is a professor of economics at Peking University. PR and YQ are employees and stockholders of Amgen Inc. Z. Zhao was an employee and stockholder of Amgen Inc. at the time of the study. JS, HB, and NW are employees of Adelphi, which received funding from Amgen Inc. to conduct this research. JDA peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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Data availability statement

The data that support the findings of this study are not publicly available due to contractual restrictions regarding their use.

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