

# The Prevalence of Weekly Angina Among Patients With Chronic Stable Angina in Primary Care Practices

## *The Coronary Artery Disease in General Practice (CADENCE) Study*

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**Background:** Angina, the cardinal symptom of coronary artery disease (CAD), is amenable to a range of therapies, and its routine assessment is considered a performance measure of quality. However, the prevalence of frequent angina among outpatients with CAD is unknown.

**Methods:** The Coronary Artery Disease in General Practice (CADENCE) Study utilized a cluster-stratified, cross-sectional design to examine angina frequency in patients with stable angina attending Australian primary care practices. The 207 participating primary care practitioners recruited 2031 consecutive patients, irrespective of the purpose of their visit. Angina frequency was quantified with the Seattle Angina Questionnaire (SAQ), and weekly angina was defined as having 1 or more episodes per week over the preceding 4 weeks [hereinafter, “weekly ( $\geq 1$ ) angina”].

**Results:** Among primary care practice patients with stable angina, 29% (95% confidence interval [CI], 26%-31%) experienced weekly ( $\geq 1$ ) angina, which was associated with greater physical limitations and worse quality of life (24% and 27% lower SAQ scores, respectively;  $P < .05$ )

compared with those with minimal angina (angina less than once a week over the preceding 4 weeks). The proportion of patients with weekly ( $\geq 1$ ) angina within a clinic ranged from none (14% of clinics) to more than 50% (18% of clinics). Patient characteristics associated with weekly ( $\geq 1$ ) angina included female sex (odds ratio [OR], 1.42; 95% CI, 1.13-1.78), a history of heart failure (OR, 1.59; 95% CI, 1.22-2.08), and peripheral artery disease (OR 1.89; 95% CI, 1.42-2.51;  $P < .001$  for all comparisons).

**Conclusions:** Almost 1 in 3 patients with stable angina attending primary care practices had angina at least once a week, which was associated with worse quality of life. Moreover, weekly ( $\geq 1$ ) angina varied considerably across clinics, possibly reflecting variability in the identification and management of angina. The potential role of an angina performance measure to improve patients' outcomes, including symptom control, warrants further consideration.

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**T**HE MAJOR CLINICAL MANIFESTATIONS of coronary artery disease (CAD) include acute coronary syndromes (ACS) and chronic stable angina.

Although ACS typically result in hospital admission and are therefore readily identified through administrative data or national registries,<sup>1-3</sup> the more prevalent condition of chronic stable angina is predominantly managed in the outpatient setting where data are less readily available. Those that are available are often derived from hospital specialist clinics<sup>4</sup> or follow-up of hospital-based ACS registries<sup>5,6</sup> and may not reflect the status of patients' angina in primary care practices.

Management of chronic stable angina involves both the secondary prevention of

cardiovascular events through risk reduction (eg, antiplatelet agents, statins) and the optimization of patients' health status by minimizing anginal symptoms with antianginal medications or coronary revascularization. Although therapeutic guidelines<sup>7-9</sup> and performance measures<sup>10</sup> are well developed for preventing cardiovascular events in patients with CAD, there are no outcomes-based performance measures for anginal control, despite a range of well-established therapies<sup>7-9,11</sup> and anginal status being associated with ACS hospitalizations and mortality.<sup>12</sup> Substantial barriers preventing the promotion of angina control as an outcome measure of health care quality in stable angina include limited insight into the current success of angina manage-

### Primary Definitions

**Myocardial infarction** is defined by any of the following criteria:

1. Clinical diagnosis: rest angina >20 minutes, new ST/T changes and troponin rise
2. Hospital discharge diagnosis of myocardial infarction
3. Electrocardiogram evidence of pathological Q waves ( $\geq 1$  mm in 2 contiguous leads)
4. Patient report

**Unstable angina** is defined by either of the following criteria:

1. Clinical diagnosis: rest angina >20 minutes, new ST/T changes, and no troponin rise
2. Hospital discharge diagnosis of unstable angina

**Canadian Cardiovascular Society Classification (CCSC)** defines the functional impairment produced by the angina with patients categorized by 1 of the following:

1. Ordinary physical activity (eg, walking, climbing stairs) does not cause angina
2. Slight limitation of ordinary (eg, angina when walking or climbing stairs rapidly)
3. Marked limitation of ordinary activity (eg, angina with 1 flight of stairs at normal pace)
4. Inability to perform any physical activity without discomfort

**Cardiac failure** is defined by either of the following criteria:

1. Clinical diagnosis: including both symptoms and signs of heart failure and objective evidence of cardiac (systolic or diastolic) dysfunction
2. Hospital discharge diagnosis of heart failure or acute pulmonary edema

**Hypercholesterolemia** is defined by either of the following criteria:

1. Clinical diagnosis: low-density lipoprotein cholesterol level  $\geq 77$  mg/dL in the absence of lipid-lowering therapy
2. Initiation of pharmacological lipid-lowering therapy

**Hypertension** is defined as the initiation of pharmacological antihypertensive therapy

**Diabetes mellitus** is defined as the biochemical confirmation of diabetes mellitus

**Peripheral artery disease/Raynaud disease** is defined by either of the following criteria:

1. Clinical diagnosis by a medical practitioner of either of these disorders
2. Imaging studies revealing evidence of  $\geq 50\%$  stenosis in a vascular bed
3. Imaging studies revealing evidence of an aneurysm

**Asthma and COPD** are defined as a previous clinical diagnosis of either of these and the current use of bronchodilator therapy

### Derived Definitions

**ACP criteria for angina pectoris** includes:

1. Substernal chest discomfort with a characteristic quality and duration
2. Provoked by exertion or emotional stress
3. Relieved by rest or sublingual nitrates\*

"Typical angina" is defined by all 3 criteria, "atypical angina" if only 2 criteria are met

**Confirmed CAD** is defined as a history of any of the following:

1. Documented myocardial infarction
2. Hospital admission for unstable angina
3. Coronary revascularization (ie, angioplasty/stenting or coronary artery bypass graft)
4. Positive cardiac diagnostic test for myocardial ischemia/CAD (ie, exercise test, myocardial scintigraphy, stress echo or angiography)

"**Weekly angina**" is defined as angina occurring at least once per week in the month preceding the study visit, based on patient responses to the SAQ.

"**Minimal angina**" is defined as angina occurring less than once per week in the month preceding the study visit, based on patient responses to the SAQ.

**Figure 1.** Study definitions. ACP indicates American College of Physicians; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; SAQ, Seattle Angina Questionnaire. ST/T refers to the ST segment and T wave on the electrocardiogram. The asterisk indicates the study by Diamond.<sup>19</sup> (To convert low-density lipoprotein cholesterol to millimoles per liter, multiply by 0.0259.)

ment (eg, do outpatients with CAD have much angina?) and variability of angina control (eg, do some clinicians manage their patients' angina well while others do not?). To address these gaps, we sought to determine the extent and variability of anginal burden among general practitioners' (GPs) clinics and its association with patients' quality of life.

The Coronary Artery Disease in General Practice (CADENCE) Study was established to profile the health and management of patients with chronic stable angina in a nationally representative sample of primary care practices in Australia. The primary objective was to determine the proportion of patients with frequent angina, de-

spite active management. Secondary objectives included (1) assessing the impact of frequent angina on quality-of-life measures, (2) identifying discrepancies between patients' and clinicians' assessment of anginal control, and (3) evaluating the heterogeneity in the extent of anginal control between clinics.

## METHODS

The CADENCE Study was a cluster-stratified, cross-sectional survey of patients with a clinical diagnosis of angina attending GPs' practices throughout Australia. The study was registered with the Australian and New Zealand Clinical Trials Registry and was approved by the Royal Australian College of GPs National Research and Evaluation Ethics Committee, with all participating patients providing written informed consent.

### GP RECRUITMENT

The CADENCE study sought to include GPs in proportion to the population of Australian residents, with particular attention to state/territory and urban/rural settings. In August 2006, all of the 19 817 registered GPs in Australia (database from Dendrite, Sydney) were contacted by mail inviting expressions of interest (EOIs). The EOIs contained the GP practice location and nomination as an urban/rural practice was cross-referenced against the Rural, Remote, and Metropolitan Area categories database. To ensure geographic representation of practices, GPs were selected in ratios proportional to the census population by (1) state population (8 Australian states and territories) and (2) urban and rural location within each state, thereby constituting 16 strata nationally (Australian Bureau of Statistics, 2001 data<sup>13-18</sup>). Any strata not receiving sufficient EOIs were remailed, up to a maximum of 3 times. We received EOIs from 535 GPs in total, and 6 of the 16 strata (most of which were rural) remained underrepresented. To encourage participation, GPs were eligible for continuing professional development points. The EOIs exceeding planned strata allocations ( $n=53$ ; predominately urban) were held in reserve as potential replacements in the event of investigator withdrawal in the same geographic stratum.

### PATIENT RECRUITMENT WITHIN PRACTICES

From October 2006 through March 2007, each selected GP prospectively recruited 10 to 15 consecutive adults with a history of angina, irrespective of the reason for their consultation. The inclusion criteria for patient recruitment were (1) age of 18 years or older and (2) a clinical diagnosis of stable angina, defined as ever experiencing a substernal chest discomfort (typically "squeezing," "tightness," or "heaviness") usually persisting for a few minutes. Importantly, patients were recruited consecutively and not required to have ongoing anginal symptoms. Patients were excluded if they were unable to complete a written questionnaire or provide informed consent in English.

### DATA COLLECTION AND DEFINITIONS

For each patient recruited, a case report form containing details of their cardiac history, coronary risk factors, associated medical conditions, and current medications was completed by the GP. **Figure 1** summarizes the definitions supplied to the GPs for each study element. Based on this data, the study population was further categorized using the American College of Physicians (ACP) angina criteria and by objective clinical and diagnostic criteria for the presence of CAD (confirmed CAD) (Figure 1).

The GPs were asked to assess patients' anginal symptoms using the Canadian Cardiovascular Society Classification (CCSC).<sup>20</sup> They were also explicitly asked whether the patients' angina was "optimally controlled." Independent of GP-derived assessments, patients completed the Seattle Angina Questionnaire (SAQ), a well-established and validated disease-specific quality-of-life instrument for patients with CAD that fulfills current performance measures for quantifying patients' symptoms and function.<sup>21,22</sup> The SAQ independently quantifies 5 clinically important domains of coronary disease: the frequency of angina, whether a recent change in symptoms has occurred over the past month, patients' physical limitations, their quality of life, and their satisfaction with the current treatment of their angina.

The primary end point of the study was the prevalence of weekly angina, which was defined as 1 or more episodes of angina per week in the 4 weeks preceding recruitment [hereinafter, "weekly ( $\geq 1$ ) angina"], as recorded by the angina frequency domain of the SAQ. This was defined a priori for the study, on the basis of clinical judgment and previous demonstration of improved quality of life after revascularization therapy among patients with weekly ( $\geq 1$ ) angina before their procedure.<sup>23</sup>

### SAMPLE SIZE CALCULATION

No previous estimates of weekly ( $\geq 1$ ) angina prevalence were available in primary care settings; however, estimates from a tertiary clinic setting in Seattle, Washington,<sup>24</sup> and an international clinical trial<sup>25</sup> were 46% and 29%, respectively. The sample size calculations were based on an estimated median prevalence of weekly ( $\geq 1$ ) angina of 38%.

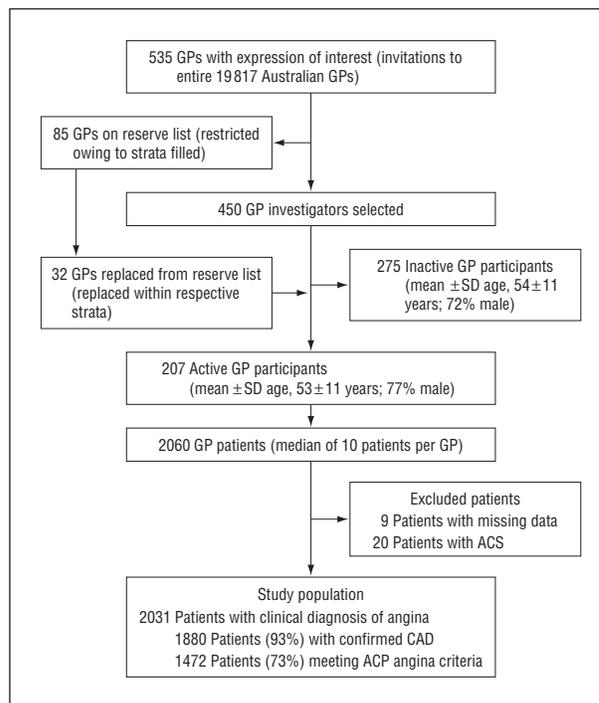
The study design of CADENCE (stratification by state, followed by urban/rural location and clustered by GP) was considered in sample size calculations because stratification typically reduces variance and clustering increases it.<sup>26</sup> Because no previous variance estimates were available, sample size was calculated assuming simple random sampling and was multiplied by a design effect.<sup>26</sup> Using a modest design effect of 4.6, a sample size of 3000 patients was required to achieve 95% confidence intervals (CIs) within 10% (relative) for a 38% prevalence. To recruit the 3000 patients, we aimed to enroll 450 GPs into the prespecified 16 strata.

### DATA ANALYSIS

For all estimates and analyses, the complete available data set was used with no imputation for missing values. Frequency data were expressed relative to the number of patients available for each variable. The CIs were produced using SAS statistical software (version 9.1; SAS Institute, Cary North Carolina), accounting for the stratified (ie, 16 state and urban/rural strata), clustered (ie, 207 GP clusters) survey design.

Comparisons between patients with weekly ( $\geq 1$ ) angina and minimal angina [defined as angina less than once a week over the preceding 4 weeks, hereinafter, "minimal ( $< 1$ ) angina"] were performed using a general linear model with weekly ( $\geq 1$ )/minimal ( $< 1$ ) angina as a categorical predictor variable and the clinical or other SAQ variables being either binary or continuous. The difference between means for each group was estimated, and a *P* value was determined (using a *t* test) using a variance estimate accounting for the survey design.

A logistic regression model was fitted to explore 6 factors (sex, age, heart failure, smoking status, diabetes mellitus, and the presence of peripheral artery disease) selected a priori to potentially be associated with weekly ( $\geq 1$ ) angina. The stratified clustered survey design was incorporated into the estimation of CIs and *P* values. Each term was fitted individually in a



**Figure 2.** Summary of patient study recruitment. ACP indicates American College of Physicians; ACS, acute coronary syndromes; CAD, coronary artery disease; GP, general practitioner.

univariate model. Terms that were significant at the  $P < .10$  level<sup>27</sup> were then entered together in a multivariable model. In addition, a multivariable model with all terms was fitted to ensure that no relevant factors were omitted. The final odds ratios (ORs) (with 95% CIs) and *P* values are reported.

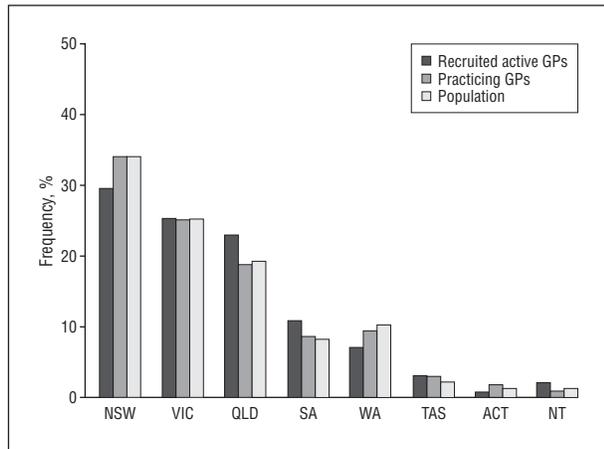
## RESULTS

### STUDY POPULATION

Of 450 selected GPs, 32 withdrew prior to collecting data and were replaced by previously unselected EOIs from the same geographic strata. The 207 active GPs who submitted data within the study recruitment period (**Figure 2**) had a geographic distribution comparable with that of the Australian GP population and the adult Australian population for each state (**Figure 3**). However, compared with the Australian GP population, active GPs in the CADENCE Study were more often older than 55 years (33% vs 42%, respectively;  $P = .01$ ), overseas graduates (28% vs 44%;  $P < .001$ ), and in rural practice (26% vs 38%;  $P < .001$ ).

Participating GPs recruited between 1 and 15 patients, with a median of 10 (interquartile range, 9-12) patients. Nine recruited patients were excluded owing to insufficient data. To ensure that only patients with chronic stable angina were considered, an additional 20 patients with a de novo ACS presentation (ie, no history of chronic angina) were excluded. Thus, a total of 2031 patients with chronic stable angina formed the final study population.

Supporting the accuracy of a stable angina diagnosis, objective evidence of CAD (confirmed CAD) (Figure 1) was documented in 93% of patients, based on prior ACS



**Figure 3.** The state-by-state distribution of general practitioners (GPs) participating in the study (recruited active GPs), those practicing within Australia as per the Australian Institute of Health and Aging (practicing GPs), and the Australian population distribution from census data (population). Frequencies are expressed with respect to the total national numbers for each group, thus the sum of all regions totals 100%. NSW indicates New South Wales; Vic, Victoria; QLD, Queensland; SA, South Australia; WA, Western Australia; TAS, Tasmania; ACT, Australian Capital Territory; NT, Northern Territory.

(76%), revascularization (67%), or diagnostic cardiac investigation (87%). Moreover, 73% of patients fulfilled the ACP criteria for angina. Importantly, the stability of patients' angina symptoms was confirmed by a mean (SD) SAQ Angina stability score (where a score of 50 indicates no change over the prior 4 weeks and higher scores indicate improved angina control) of 62 (26), suggesting that, on average, patients' symptoms were stable or improving at the time of enrollment.

### CHARACTERISTICS OF PATIENTS WITH CHRONIC STABLE ANGINA IN PRIMARY CARE PRACTICES

The mean (SD) patient age was 71 (11) years with 63% being male (**Table 1**). Patients had a mean time from original diagnosis of more than 8 years, with 54% diagnosed more than 5 years previously. Almost 90% of the study patients had previously seen a cardiologist, with 62% having had cardiac consultation within the preceding 12 months. Of those patients with chronic stable angina who had never seen a cardiologist, 28% were experiencing angina at least weekly (compared with 29% for those who had previously seen a cardiologist;  $P = .66$ ).

The primary outcome of the study was the prevalence of weekly ( $\geq 1$ ) angina, which was present in 29% (95% CI, 26%-31%) of the cohort. This included patients experiencing daily episodes (7%) and those experiencing angina at least once a week but not daily (22%). Furthermore, in the preceding 4 weeks, 52% had not experienced any angina, and 18% had episodes less than once a week (ie, monthly only). There was a close relationship between the frequency of angina and patients' perceptions of their quality of life, as assessed by the SAQ physical limitation and quality-of-life scales, underscoring the important association between angina and patient health status (**Figure 4A**).

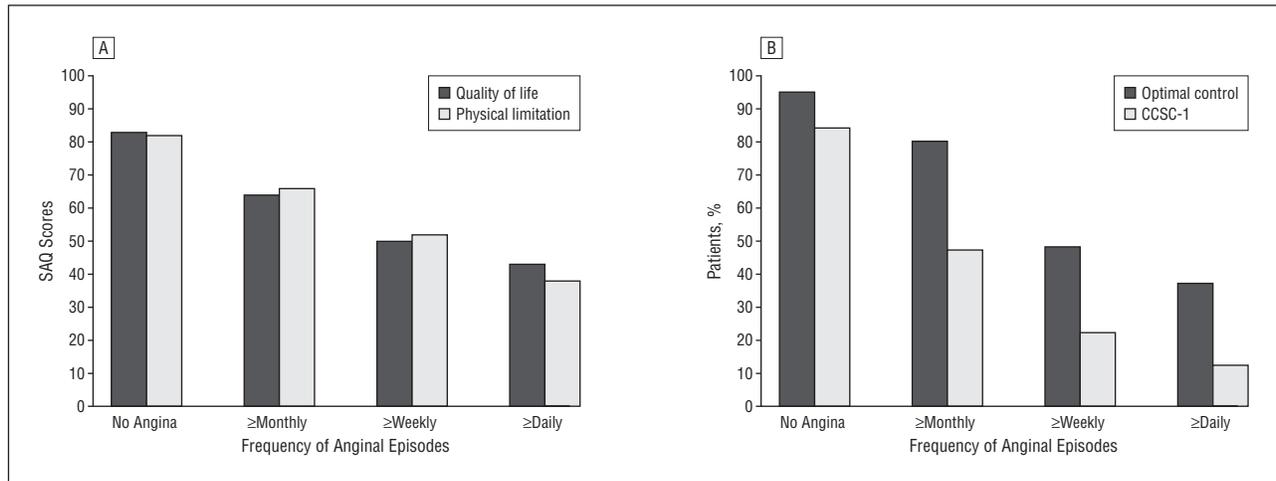
**Table 1. Clinical Features of Study Population<sup>a</sup>**

| Clinical Feature  | % or Mean $\pm$ SD (Patient Data Available, No.) |
|---|--|
| Age, y  | 71 $\pm$ 11 (1996)                               |
| Male sex  | 64 (2005)  |
| Angina characteristics  |  |
| Substernal chest discomfort   | 93 (1815)  |
| Pain provoked by exertion   | 73 (1815)  |
| Pain provoked by emotional stress   | 26 (1815)  |
| Pain relieved by rest   | 54 (1815)  |
| Pain relieved by sublingual nitrates  | 51 (1815)  |
| Risk factors and associated conditions  |  |
| Hypercholesterolemia  | 78 (1939)  |
| Hypertension  | 72 (1934)  |
| Diabetes mellitus   | 30 (1999)  |
| Smoking history, past or current  | 59 (1995)  |
| Total cholesterol, mg/dL  | 169.8 $\pm$ 50.2 (1955)                          |
| HbA <sub>1c</sub> level in patients with diabetes mellitus, % of total hemoglobin | 7.2 $\pm$ 3.2 (583)                              |
| Systolic blood pressure, mm Hg  | 129 $\pm$ 16 (2009)                              |
| Diastolic blood pressure, mm Hg   | 74 $\pm$ 10 (2010)                               |
| Previous events   |  |
| Unstable angina   | 45 (2004)  |
| Myocardial infarction   | 47 (2004)  |
| Acute pulmonary edema   | 14 (1960)  |
| Other disorders   |  |
| Atrial fibrillation   | 10 (1347)  |
| Cardiac failure   | 22 (2002)  |
| Peripheral artery disease   | 17 (1533)  |
| Asthma/COPD   | 22 (1873)  |
| Chronic stable angina management  |  |
| Review by cardiologist  | 89 (2017)  |
| Antiplatelet agent(s)   | 82 (2016)  |
| Statin  | 82 (2017)  |
| Angiotensin-converting enzyme inhibitor   | 50 (2006)  |
| $\beta$ -Blocker  | 53 (2007)  |
| Long-acting nitrate   | 39 (2009)  |
| Calcium channel blocker   | 34 (1984)  |
| Other antianginal(s)  | 8 (1980)   |
| Coronary angioplasty/stenting   | 41 (1986)  |
| Coronary artery bypass grafting   | 33 (1967)  |
| Any revascularization   | 62 (1989)  |
| CCSC class  |  |
| I   | 61 (1953)  |
| II  | 29 (1953)  |
| III   | 8 (1953)   |
| IV  | 2 (1953)   |
| SAQ domains   |  |
| Angina frequency  | 84 $\pm$ 23 (1983)                               |
| Angina stability  | 63 $\pm$ 26 (1938)                               |
| Quality of life   | 70 $\pm$ 24 (1975)                               |
| Physical limitation   | 70 $\pm$ 27 (1877)                               |
| Treatment satisfaction  | 90 $\pm$ 14 (1957)                               |

Abbreviations: CCSC, Canadian Cardiovascular Society Classification; COPD, chronic obstructive pulmonary disorder; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>; SAQ, Seattle Angina Questionnaire.

SI conversion factors: To convert total cholesterol to millimoles per liter, multiply by 0.0259; to convert hemoglobin A<sub>1c</sub> to a proportion of total hemoglobin, multiply by 0.01.

A marked discordance was observed when comparing GP and patient assessments of angina control (**Figure 4B**). From the GP perspective, 61% of patients had minimal angina-related impediment in physical activity (ie, CCSC class I), including 12% of the patients who reported daily angina. More importantly, GPs considered patients' angina to be optimally controlled in 80%



**Figure 4.** Relationship between angina frequency and patient-assessed quality-of-life indices, and general practitioner (GP) perception. Relationship between the frequency of anginal episodes (over the preceding 4 weeks) and (A) patient-assessed Seattle Angina Questionnaire (SAQ) quality-of-life indices or (B) GP-perceived physical limitation by angina (Canadian Cardiovascular Society Classification 1 [CCSC-1]) and optimal therapeutic control.

of cases, despite the prevalence of frequent angina. Among the patients with weekly ( $\geq 1$ ) and daily angina, GPs felt that 48% and 37%, respectively, were optimally controlled (Figure 4B).

#### PREDICTORS OF WEEKLY ( $\geq 1$ ) ANGINA

Compared with patients with minimal ( $< 1$ ) angina, those with weekly ( $\geq 1$ ) angina were more often female, current smokers, and had a history of cardiac failure, peripheral artery disease, or chronic obstructive airway disease (Table 2). Patients with weekly ( $\geq 1$ ) angina were more likely to be prescribed antianginal therapy and less likely to have undergone coronary artery bypass grafting (Table 2). Importantly, there were no differences between groups in age, risk factors other than smoking, previous ACS, atrial fibrillation, duration of diagnosis, cardiologist consultation, use of cardio-protective therapies, or prior percutaneous coronary interventions. Comparison of patient-assessed SAQ health status domains demonstrates that patients who experienced weekly ( $\geq 1$ ) angina were more impaired, with 27% lower SAQ quality-of-life scores, 24% lower physical limitation scores, and 9% lower ratings of treatment satisfaction ( $P < .001$  for all comparisons) (Figure 5A). Although GPs often classified patients with weekly ( $\geq 1$ ) angina as having CCSC class I or II, the relative proportion of those with weekly ( $\geq 1$ ) angina increased in the higher CCSC classes (Figure 5B). Despite this, GPs considered that 53% of patients with weekly ( $\geq 1$ ) angina were optimally controlled [compared with 92% among those with minimal ( $< 1$ ) angina;  $P < .001$ ].

The 6 potential determinants of weekly ( $\geq 1$ ) angina were individually assessed in both univariate and multivariable logistic regression models, adjusting variance for the stratified cluster survey design. The same factors were statistically significant in both models and included (OR and 95% CI; in multivariate model, respectively): female sex (OR, 1.42; 95% CI, 1.13-1.78;  $P < .003$ ), a history of heart failure (OR, 1.59; 95% CI, 1.22-2.08;  $P < .001$ ), and peripheral artery disease (OR, 1.89; 95%

CI, 1.42-2.51;  $P < .001$ ). The predictive accuracy as measured by the C statistic was 0.60.

#### VARIABILITY IN ANGINA FREQUENCY CONTROL ACROSS GP CLINICS

Given the prevalence of weekly ( $\geq 1$ ) angina and the strong association of angina frequency with patients' SAQ-assessed quality of life, we examined the frequency of weekly ( $\geq 1$ ) angina across GP clinics. We found marked variability in angina control across the 207 clinics, ranging from none [0% of a GP's patients having weekly ( $\geq 1$ ) angina] to all [100% of the GP's patients having weekly ( $\geq 1$ ) angina] (Figure 6). Among the GP clinics, 29 (14%) had no patients with weekly ( $\geq 1$ ) angina, whereas 35 (18%) had at least half of their patients experiencing weekly ( $\geq 1$ ) angina and 8 (4%) of clinics had all of their patients reporting weekly ( $\geq 1$ ) angina. A sensitivity analysis that included only GPs recruiting at least 10 patients showed similar variability in angina frequency control across clinics.

#### COMMENT

Patients with CAD constitute an important component of primary care and account for 1.5% of total consultations.<sup>28</sup> To our knowledge, the CADENCE Study provides the first comprehensive assessment of angina burden in a large representative sample of patients with chronic stable angina from the primary care setting. In this cluster-stratified survey, patients were consecutively recruited and needed to have a history of angina but did not require the presence of ongoing angina. In this representative population of Australian primary care patients, we found the following: (1) 29% of patients reported experiencing angina at least once a week; (2) patients with at least weekly ( $\geq 1$ ) angina had poorer function and quality of life; (3) physicians often underestimated the extent of angina and its impact on patient health status and, even among patients with fre-

**Table 2. Comparative Features of Patients With Weekly and Minimal Angina<sup>a</sup>**

| Characteristic                                    | Minimal Angina (n=1424) | Weekly Angina (n=582) |
|---|-------------------------|-----------------------|
| <b>Clinical features</b>                          |                         |                       |
| Age, mean±SD, y                                   | 71 ± 11                 | 71 ± 12               |
| Female sex <sup>b</sup>                           | 34                      | 42                    |
| Angina duration, mean±SD, y                       | 8.2 ± 8.0               | 8.0 ± 7.6             |
| Substernal chest discomfort                       | 82                      | 85                    |
| Pain provoked by exertion                         | 64                      | 68                    |
| Pain provoked by emotional stress <sup>b</sup>    | 20                      | 31                    |
| Pain relieved by rest <sup>b</sup>                | 47                      | 52                    |
| Pain relieved by sublingual nitrates <sup>b</sup> | 40                      | 57                    |
| <b>Risk factors</b>                               |                         |                       |
| Hypercholesterolemia                              | 78                      | 77                    |
| Hypertension                                      | 72                      | 73                    |
| Diabetes mellitus                                 | 29                      | 32                    |
| Current smoker <sup>b</sup>                       | 15                      | 22                    |
| <b>Events/comorbidities</b>                       |                         |                       |
| Previous unstable angina/infarction               | 70                      | 71                    |
| Clinical heart failure <sup>b</sup>               | 19                      | 28                    |
| Peripheral artery disease <sup>b</sup>            | 14                      | 25                    |
| Asthma/obstructive airway disease <sup>b</sup>    | 19                      | 30                    |
| <b>Clinical management</b>                        |                         |                       |
| Antiplatelet agent(s)                             | 81                      | 82                    |
| Statin  | 82                      | 81                    |
| Angiotensin-converting enzyme inhibitor           | 50                      | 50                    |
| Angiotensin receptor blocker                      | 23                      | 24                    |
| β-Blocker   | 53                      | 54                    |
| Long-acting nitrate <sup>b</sup>                  | 32                      | 54                    |
| Calcium channel blocker <sup>b</sup>              | 33                      | 38                    |
| Other antianginal agents <sup>b</sup>             | 5                       | 14                    |
| Coronary angioplasty/stenting                     | 40                      | 44                    |
| Coronary artery bypass grafting <sup>b</sup>      | 34                      | 30                    |

<sup>a</sup>Weekly angina indicates 1 or more episodes of angina per week, and minimal angina indicates less than 1 episode of angina per week over the preceding 4 weeks.

<sup>b</sup>*P* < .05 for minimal vs weekly angina.

quent angina, frequently felt that their patients' angina was optimally controlled; (4) there was considerable variability among GP clinics in angina control, ranging from 0% to 100% of practices' patients experiencing at least weekly ( $\geq 1$ ) angina and almost 1 in 5 clinics having more than half of their patients experiencing angina at least once a week; and (5) that women, those with heart failure, and those with peripheral artery disease were considerably more likely to report weekly ( $\geq 1$ ) angina. The prevalence, consequences, and variability (with presumed opportunity for improvement), argue strongly that reproducible estimates of angina could be a valuable outcome measure of quality for outpatients with CAD.

#### ANGINAL CONTROL IN OUTPATIENT POPULATIONS

We could identify only 1 other study that previously assessed angina frequency in solely general practice outpatient clinics. Garratt et al<sup>29</sup> used the SAQ in 655 patients with stable angina from 12 primary care practices in Northern England. Despite similarities in age and sex to the CADENCE Study cohort, SAQ scores were considerably lower in their study (mean [SD] angina fre-

quency, 67 [27]; angina stability, 54 [24]; quality of life, 59 [23]; physical limitation, 37 [19]; and treatment satisfaction, 84 [13]), suggesting even worse angina control than that observed in our Australian clinics. Discovering the prevalence of frequent angina in both studies underscores the opportunity to discover highly symptomatic patients among outpatients with CAD and to identify those who might benefit from more intensive treatment in primary care settings.

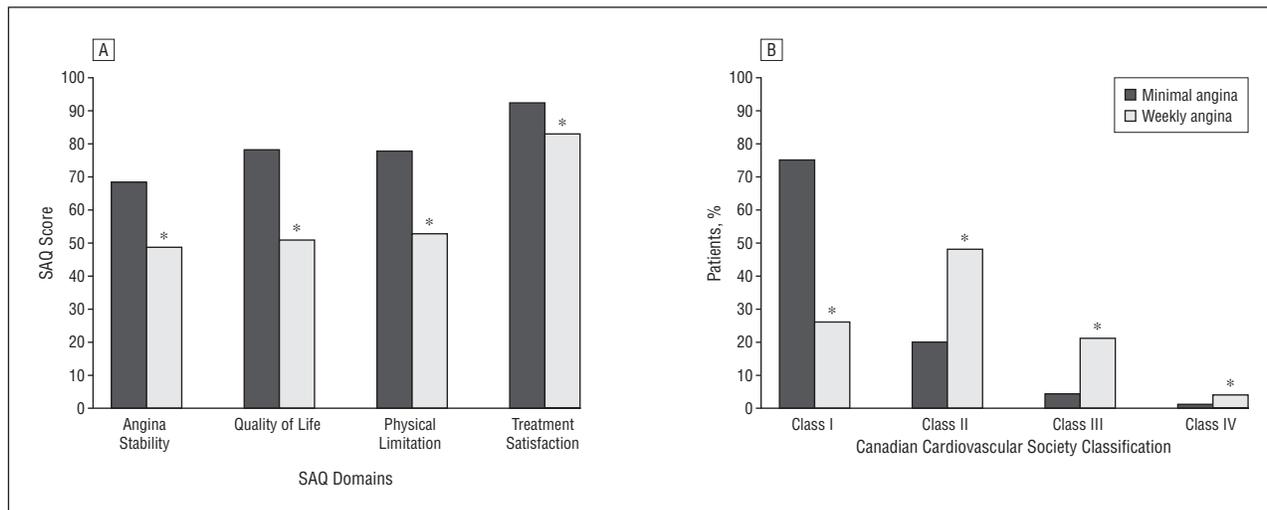
Several hospital/specialist-based studies have also reported frequent angina among outpatients with CAD. Wiest et al<sup>30</sup> reported that 30% of their 7038 outpatients (from 7 US Veterans Affairs medical centers) experienced at least 2 episodes of angina per week, and Spertus et al<sup>24</sup> found that 46% of 4484 outpatients with CAD (from 6 US Veterans Affairs medical centers) experienced weekly angina. Similarly Kirwan et al<sup>31</sup> found that 29% of the ACTION Study patients had at least 1 episode of angina per week when assessed at 293 centers. The prevalence of frequent angina in these hospital clinics is similar to that found in the CADENCE Study, further supporting that frequent angina is common, although none of these prior reports noted the discrepancy between patients' and physicians' assessments of symptom control. Because patients with weekly ( $\geq 1$ ) angina have an impaired quality of life and are at higher risk of cardiovascular events,<sup>24</sup> strategies that improve angina control may potentially improve quality of life and reduce cardiovascular events and warrant further investigation.

#### CLINICIAN ASSESSMENT OF PATIENTS WITH ANGINA

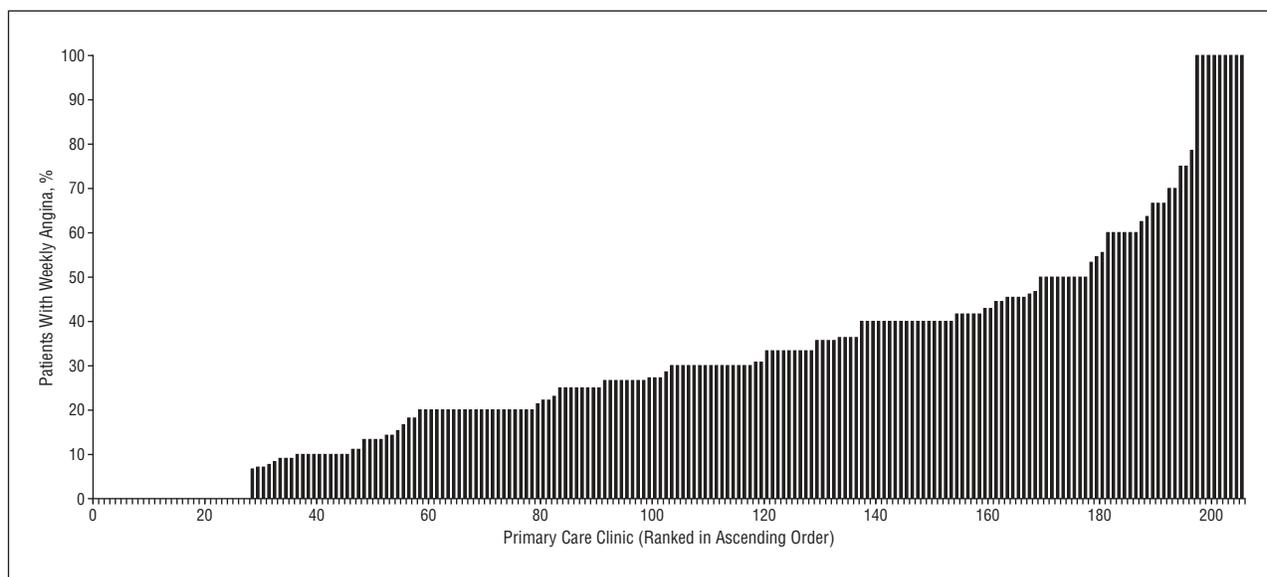
Although multiple factors are responsible for the prevalence of frequent angina in patients with CAD, an important factor is likely to be clinicians' limited awareness of the angina burden experienced by their patients. In the CADENCE Study, GPs reported that angina was optimally controlled in 80% of their patients and that 61% had minimal angina-related impediment in their physical activity (CCSC class I). In contrast, only 52% of patients reported being angina-free, and only 47% reported that their angina had not limited their enjoyment of life. We hypothesize that clinicians' underestimation of angina frequency and its impact on quality of life is partially responsible for the prevalence of angina and that more intensive treatment could minimize both angina symptoms and its impact on patients' health-related quality of life. Systematically assessing and reporting angina frequency as a performance measure could be advantageous in that it would alert clinicians to the presence of frequent angina symptoms and identify those patients who require more intensive treatment.

#### ANGINAL PERFORMANCE MEASURES

To achieve optimal outcomes in patients with CAD, attention needs to focus not only on disease progression (ie, cardiovascular events) but also on patients' health status, including their symptoms, function, and health-related quality of life.<sup>32</sup> The creation of a performance measure for symptom frequency, as assessed by patients rather than clinicians, could be an important step toward im-



**Figure 5.** Differences between patients with minimal angina (<1 episode per week over the preceding 4 weeks) and weekly ( $\geq 1$  episodes per week) angina in quality-of-life indices. Comparisons between patients with minimal (<1) angina and weekly ( $\geq 1$ ) angina in (A) the Seattle Angina Questionnaire (SAQ), a patient-derived quality-of-life instrument, and (B) the Canadian Cardiovascular Society classification, a physician-assigned quality-of-life assessment. The asterisk indicates  $P < .001$  compared with minimal angina.



**Figure 6.** Prevalence of weekly angina ( $\geq 1$  episodes per week) among Australian primary care clinics.

proving care. Enabling feedback to health care providers on the control of their patients' symptoms could lead to quality improvement efforts that may include intensification of medical regimens or referral for coronary revascularization, as endorsed by clinical guidelines. This paradigm has been well developed for ACS, for which explicit measurement of performance and the creation of national quality improvement campaigns (eg, door-to-balloon [D2B] times<sup>33-35</sup> and use of  $\beta$ -blockers<sup>36</sup>) have been associated with improved performance.

In chronic stable angina, clinical guidelines<sup>7,8</sup> and performance measures<sup>10</sup> have been developed for reducing cardiovascular events. However, there are no established performance measures for patient-centered, health status outcomes, despite guidelines detailing multiple therapies for symptom control.<sup>22</sup> The CADENCE Study provides the initial foundations for the multiple criteria required to de-

velop a performance measure for angina control,<sup>37</sup> including documentation of impaired health status in a considerable proportion of patients with stable angina and substantial variability among GP clinics in controlling angina frequency. Thus, using analytical strategies similar to those comparing D2B times among different hospitals, comparing GP practices may identify system-level, access to care, and treatment barriers that prevent optimal patient outcomes. Such efforts could also reduce the sex disparity observed in the CADENCE Study. One emerging opportunity to test the benefits of such a performance measure is the recently developed Improving Continuous Cardiac Care (IC3) program,<sup>38</sup> a data collection program developed by the National Cardiovascular Data Registry to aid clinicians in applying American College of Cardiology/American Heart Association–endorsed clinical guidelines and performance measures within their practice. With ap-

appropriate performance measures, this program could make substantial strides toward achieving the Institute of Medicine's goals for a higher quality, more equitable, and patient-centered health care system.<sup>39</sup>

### STUDY LIMITATIONS AND FUTURE DIRECTIONS

Results of this study should be considered in light of the following potential limitations. First, although we achieved a balance of GP clinics that reflected the population of Australia, participation in the CADENCE Study was voluntary, and control of patient angina may differ substantially among clinics that did and did not participate. Speculatively, participants who voluntarily chose to enroll their patients may have been more confident in the management of their patients' angina, and the prevalence among non-participants may be worse than that found in this study. Second, the ideal therapeutic goal is for patients to be angina-free, which will not be achievable in all patients. We used clinical intuition to focus on weekly ( $\geq 1$ ) angina as the threshold to define good and poor control of angina symptoms. Potential clinical benchmarks could include no, monthly, weekly, or daily angina. Because we found a linear relationship between angina frequency and the quality of life, without a clear threshold effect, we acknowledge that our threshold was arbitrary, and professional consensus will be needed to define optimal targets for angina control. Third, from the initial sample-size estimates a target population of 3000 was calculated, but only 2031 were recruited. However, post hoc power calculations revealed that we had considerably overestimated the study design effect, having assigned a value of 4.6 when, in fact, it was 1.56. This is evident in the narrow 95% CIs achieved (half of what had originally been estimated) in the primary end point, providing us with adequate power to conduct our analyses. Finally, we were unable to develop a robust risk-adjustment model to account for patient variability in angina control so that residual variability (presumably attributable to the clinical care provided or unmeasured patient characteristics) could be determined. Accordingly, we believe that the quantification and benchmarking of the health status of patients with CAD is valuable for internal quality improvement but is not yet amenable to public reporting and accountability.<sup>40</sup>

In conclusion, the CADENCE Study has provided important insights into the angina burden of patients with chronic stable angina in primary care and clearly defined the potential for patient-centered health status assessments as performance measures to quantify and improve quality of care in these patients. Further research work is needed to define how best to measure angina, what reasonable target levels and reporting metrics should be, how best to risk-adjust performance, and to develop strategies that can improve patients' symptoms, function, and quality of life.<sup>37</sup> In the interim, clinicians should take heed and closely assess angina frequency and its impact on their patients.

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