Sta*B*le angina: pe*R*cept*I*on of nee*D*s, quality of life and mana*G*em*E*nt of patients (BRIDGE study) - a multi-national European physician survey

Giuseppe Ambrosio, MD, PhD, FACC, FESC1, Peter Collins, MA, MD, FRCP, FESC, FACC2,3, Ralf Dechend, MD4,5, Jose Lopez-Sendon, MD, PhD6, Athanasios J. Manolis, MD, FESC, FACC, FAHA7 , A. John Camm, MD, FMedSci, FRCP, FESC2,8

1 Division of Cardiology, University of Perugia School of Medicine, Perugia, Italy

2 Imperial College London, London, United Kingdom

3 Royal Brompton Hospital, London, United Kingdom

4 Experimental and Clinical Research Center, a joint cooperation between the Max-Delbrück Center for Molecular Medicine and the Charité Medical Faculty, Berlin, Germany

5 HELIOS-Clinic, Berlin, Germany

6 Cardiology, Hospital Universitario La Paz, IdiPaz, Madrid, Spain

7 Department of Cardiology, Asklepeion General Hospital, Athens, Greece

8 Cardiology Clinical Academic Group, Molecular & Clinical Sciences Institute, St. George’s University of London, London, United Kingdom

**Corresponding author**

Athanasios J. Manolis, tel: +30 6944 946394, e-mail: ajmanol@otenet.gr, fax: +30 213 216 3209

**E-mails of authors**

G Ambrosio: giuseppe.ambrosio@ospedale.perugia.it

P Collins: peter.collins@imperial.ac.uk

R Dechend: ralf.dechend@charite.de

J Lopez-Sendon: jlopezsendon@gmail.com

AJ Manolis: ajmanol@otenet.gr

AJ Camm: jcamm@sgul.ac.uk

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# Abstract

Stable angina (SA) is a chronic condition reducing physical activity and quality of life (QoL). Physicians treating patients with SA in, Italy, Germany, Spain, and United Kingdom completed a web-based survey. The objective was to assess physician perceptions of patient needs, the impact of SA on QoL and evaluate SA management. Overall, 659 physicians (cardiologists and general practitioners (GPs)) entered data from 1965 eligible patients. The perceived importance of everyday activities for patients with a recent diagnosis (≤2 years) was higher than for patients with a longer diagnosis (>2 years), while severity of limitations for those activities that were rated similarly for both groups. Gender-based analyses revealed that physicians documented more severe SA, more symptoms and more angina attacks in women, yet they rated the patients’ condition as similar for both sexes. Women also received less medical and interventional treatment. Patients who previously had had a percutaneous coronary intervention (PCI) had more severe SA, despite more intense medical treatment, than patients with no previous PCI. In conclusion, severity, symptoms and impact of SA on health status and everyday life activities vary by duration of disease, gender and previous PCI. However, physicians do not seem to attach importance to these differences.

# Introduction

Stable angina (SA) is a debilitating condition that limits physical activity and reduces quality of life (QoL).[1](#_ENREF_1), [2](#_ENREF_2) In Europe and the United States, the prevalence of SA in the general population is estimated to be about 2-4%.[3](#_ENREF_3), [4](#_ENREF_4)

Despite available treatment options, including lifestyle modifications, medical therapy, and coronary revascularization,[5](#_ENREF_5) a considerable proportion of patients with SA experience recurring angina attacks.[1](#_ENREF_1), [2](#_ENREF_2) Patients with more frequent angina experience greater physical limitations and lower self-reported QoL.[2](#_ENREF_2)

Since angina cannot be objectively assessed by laboratory or imaging tests, treatment decisions are largely guided by the physician’s assessment of the burden of symptoms in individual patients.[6](#_ENREF_6) This could potentially lead to sub-optimal treatment, because the frequency of angina and its impact on QoL are often under-estimated by physicians.[2](#_ENREF_2), [6](#_ENREF_6) In the cross-sectional APPEAR study, the frequency of angina was under-estimated by physicians in 42% of the cases.[6](#_ENREF_6) In the cross-sectional CADENCE survey, patients with weekly (≥1) angina episodes, and even daily angina, were considered as ‘optimally controlled’ by 48%, and 37%, of general practitioners (GPs), respectively.[2](#_ENREF_2) Poor concordance has also been shown for the perception of the severity of the condition, with patients rating their angina more debilitating, with a lower QoL compared with the physicians’ assessment.[1](#_ENREF_1)

Physicians should take QoL into consideration when treating patients with SA. To optimize treatment and allow patients to reach the best possible QoL, it is important that physicians understand which everyday activities are particularly important for the patients, what limitations they experience in those activities, and how patients perceive their health related to SA.

To assess physicians’ perceptions of SA patients’ needs, we performed a European multi-national survey on physicians treating patients with SA, evaluating the impact of SA on QoL and its management.

# Material and Methods

The BRIDGE study (Sta*B*le angina: pe*R*cept*I*on of nee*D*s, quality of life and mana*G*em*E*nt of patients) was a physician survey conducted in four European countries (Italy, Spain, Germany, United Kingdom [UK]), using computer-assisted web interviewing (CAWI), describing patients with SA as seen by their physicians.

The survey was conducted between November 2017 and January 2018. Cardiologists and GPs, hospital-based or in private practice, treating outpatients with SA were invited to participate. The physicians were part of a global panel (Lightspeed Health, London, UK) and were invited by email to take part in the CAWI survey. Physicians were eligible if they met the following inclusion criteria:

* at least 4 years (cardiologists), or 6 years (GPs) practice;
* at least 15 outpatients (cardiologists) or 40 outpatients (GPs) per week, including at least 5 patients with SA seen during the last working month;
* at least 40% of patients with SA in treatment with a therapy directly initiated by the responding physician themselves (cardiologists);
* not more than 60% of the time working in a hospital ward/day hospital (cardiologists). This restriction was not used in the UK because cardiologists are hospital-based in that country.

The physician sample was selected to cover most grouped regional geographical areas in the respective countries.

Cardiologists were asked to enter data on the last 3 patients with SA for whom they had prescribed a therapy that they decided upon, regardless of whether they began therapy on this occasion or were already on therapy for SA. GPs stating that ≥10% of the patients they saw with SA were either managed by the GP or managed by a specialist and followed by the GP on a regular basis (GP changes the therapy prescribed by the specialist) were also asked to enter the last 3 patients with SA for whom they had prescribed a therapy that they decided upon. The intention was to collect data from patients mainly managed by the GP themselves. GPs who reported that they would manage or change therapy for <10% of their patients with SA were asked to enter the last 3 patients with SA that they had seen, irrespective of a treatment decision. For these patients, socio-demographic and clinical data and information on severity and symptoms of SA, QoL related to SA and clinical management of their SA were collected (questionnaire in Supplementary Methods). The goal was to enroll at least 640 physicians (80 cardiologists and 80 GPs per country).

This was a market research study that collected only anonymized data. The survey was performed and ethics issues were addressed following the code of conduct of the European Pharmaceutical Market Research Association (EphMRA).[7](#_ENREF_7)

**Data Analysis**

Data are presented descriptively as mean (standard deviation [SD]), median (range) or % of valid cases.Statistical tests (t-test for continuous variables, chi-square test for categorical variables) were performed; information on statistical significance are provided for selected variables. Missing values were not imputed.

All patient data were analyzed for the overall study population. Subgroup analyses were performed by age groups (<65 years, 65-74 years, ≥75 years), CCS class, duration of diagnosis, gender and previous performance of a percutaneous coronary intervention (PCI). The age group <65 years was selected as a common cut-off for ‘young’ patients,[8](#_ENREF_8) while the cut-off for the two 2 age groups was selected to obtain subgroups with sufficient patient numbers for analysis.

Although the comparison between cardiologists and GPs was not an objective, the results were also compared between the patient populations entered by cardiologists and GPs.

# Results

## Physicians

A total of 318 cardiologists and 341 GPs entered data from 1977 patients (954 from cardiologists, 1023 from GPs). From this sample, 12 patients with CCS class 4 were excluded from the analysis, leaving 1965 patients for final analysis.

The 4 countries included in the study each provided approximately one-quarter of the physicians (Supplementary Table 1). The median (range) for duration of specialization was 18 (4-38 years). In the month prior to taking the survey, the physicians had seen a median of 20 outpatients with SA. Cardiologists had seen more patients (30 patients) than GPs had (15 patients).

## Patient characteristics

The majority of patients (71.8%) were men, with a mean age of 67.3 years. (Table 1). Half of the patients had CCS class 2, and most were diagnosed since 1-5 years. Compared with GPs, cardiologists saw a lower proportion of younger patients (<65 years) and a higher proportion of patients ≥75 years old, and their patients had a shorter mean time since SA diagnosis and had more often undergone PCI in the past.

**Physician perception of limitations in and importance of everyday activities for patients with recent compared with longer diagnosis of stable angina**

The importance of everyday activities for patients with recent (≤2 years) or longer (>2 years) diagnosis of SA was perceived differently by the physicians (Figure 1A).

Physicians rated the importance of all assessed everyday activities significantly higher for patients with a recent diagnosis, whereas the limitations in the same activities were rated similarly for both patient groups (Figure 1B). The only activity perceived as less limited in those patients with a longer diagnosis was intimate relationships.

Patients with a longer history of SA diagnosis were older than those with a recent diagnosis and they were less frequently in CCS class 1 and more frequently in CCS class 3, while the proportions of men and women were not different (Table 2). A sub-analysis by age group (<65 years, 65-74 years, ≥75 years) showed comparable results regarding the importance of everyday activities and the limitations SA imposes on these activities. Physicians rated the importance of everyday activities higher in patients with a recent diagnosis compared with those with a longer diagnosis in all age groups, while there were no significant differences for the degree of limitations between patients with recent and those with a longer diagnosis (Supplementary Figure 1). When the importance ratings were weighted for CCS class in the 3 age groups, the values were almost identical to the original values (Supplementary Table 3).

Overall, the observed differences in the perceived importance by time of diagnosis were similar for cardiologists and GPs (data not shown).

**Gender differences in symptoms, severity and clinical management of stable angina**

Women were slightly older than men and they had more severe disease than men based on CCS class (Table 2).

Coronary angiography and surgical interventions were performed less frequently in women compared with men (coronary angiography: 67.3 *vs* 80.1%; PCI: 37.2 *vs* 49.3%; aortocoronary bypass: 9.9 *vs* 16.8%; all p<0.05).

Current medications for the treatment of SA were also assessed. Beta-blockers were less commonly prescribed in women than in men (63.5 *vs* 70.3%; p<0.05), while long-acting nitrates were more frequently prescribed in women (46.0 *vs* 40.0%; p<0.05). There was no significant difference with respect to use of calcium antagonists, ranolazine, and ivabradine (data not shown).

In women, symptoms associated with SA (chest pain, breathing difficulties and arrhythmia/tachycardia) were more common than in men. The prevalence of symptoms such as stress/anxiety/depression was also higher in women (Figure 2A). Women reported a higher number of angina attacks per month than men (Figure 2B). This was also observed when cardiologists’ and GPs’ subsamples were analyzed separately (data not shown).

This gender difference in severity and symptoms of angina was not reflected in the physicians’ perception of their patient’s current condition. The physicians defined the patient’s condition in relation to SA as ‘not good’, ‘fair’, ‘good’ or ‘very good’ in comparable proportions of men and women (Figure 3).

**Management of stable angina in patients with and without previous PCI**

There was no age difference between patients with or without PCI, but patients with PCI had more severe disease, as shown by a higher proportion of patients with CCS class 3 compared with those without PCI (Table 2). The mean (SD) time since SA diagnosis was higher in patients with previous PCI (3.53 (2.92) years) compared with those without previous PCI (3.23 (2.89) years), with a lower proportion of patients with PCI with 1-2 years since diagnosis (27.8%) and a higher proportion of patients with 3-5 years since diagnosis (37.6%) compared with those without previous PCI (32.0% and 32.1%, respectively) (all p<0.05). The proportion of patients with previous PCI was significantly higher among patients reported by cardiologists (57%) compared with those reported by GPs (35%).

Patients with previous PCI were more frequently prescribed beta-blockers, ranolazine, and ivabradine for angina relief than those who had not undergone PCI (Figure 4).

# Discussion

This large multi-national European survey provides insight into the perception of physicians regarding SA, its management and impact on QoL. The main findings were that physicians perceived the importance of a wide range of everyday activities for patients with a recent diagnosis (≤2 years) significantly higher than for patients with a longer diagnosis (>2 years), independent of patients’ age and CCS class. Gender-based analyses showed that, according to the physicians, women had more severe SA, more symptoms and more angina attacks than men. Despite this, physicians did not perceive any difference in the current condition of their male and female patients. The frequency of medical therapies and interventions for SA differed between men and women. Finally, about half of the patients with SA had a previous PCI. The proportion was higher in patients seen by a cardiologist compared with GP patients. Those with PCI had more severe disease and received more frequently beta-blockers, ranolazine and ivabradine for angina relief. This is in line with the results of ORBITA, the first placebo-controlled PCI clinical trial showing no advantage of PCI over a sham-procedure for exercise time and angina symptoms.[9](#_ENREF_9)

## Comparability with previous studies

In this survey, patients were largely comparable to previous studies on SA with respect to age, and gender (mean 67.3 years/old, 71.8% men). The observational APPEAR study[6](#_ENREF_6) in outpatients from US cardiology practices who reported angina in the prior month and the Spanish AVANCE registry[1](#_ENREF_1) included patients 69.0 and 67.8 years/old, respectively, while patients in the Australian cross-sectional CADENCE study[2](#_ENREF_2) were older (71 years). The proportion of men in the present survey was similar to AVANCE (73.1%),[1](#_ENREF_1) but higher than in CADENCE (64%)[2](#_ENREF_2) and APPEAR (60.3%).[6](#_ENREF_6) Almost half of the patients (45.9%) were previously treated with PCI, comparable with AVANCE (47.9%)[1](#_ENREF_1) but lower than in APPEAR (57.2%).[6](#_ENREF_6) The vast majority of patients had CCS class 1 or 2 (86%), similar to those in CADENCE (90%).[2](#_ENREF_2) This suggests that overall the patient population in the present survey reflects those seen in clinical practice in many countries.

## Impact of duration of disease on physician perception

Physicians perceived the patient’s needs differently depending on the duration of the diagnosis, i.e. everyday activities were perceived to be less important to patients with longer diagnosis (>2 years) compared with those with a recent diagnosis (≤2 years). The differences in perception regarding the importance attributed to performing physical activities that were observed for patients with more recent and less recent diagnosis could be explained by the higher age of the latter.[10](#_ENREF_10) This is consistent with findings from a CADENCE sub-study, where >80 years/old patients with SA were more physically impaired by angina but had a higher QoL than younger patients.[8](#_ENREF_8) However, comparability to the present survey is limited since in CADENCE the QoL was patient-reported with the standardized Seattle Angina Questionnaire, while in our survey importance of activity and limitations was assessed by the physicians. In our survey, perception by physicians that the importance of activities was higher in patients with a recent diagnosis compared with those with a longer diagnosis was observed for most activities across age groups. Within the same age group, CCS class did not play a role in influencing physician perception of importance of activity either. Therefore, physicians may tend to assume that over time patients get used to their condition, and therefore those with a longer diagnosis rate physical activities as less important.

Although direct comparison between cardiologists and GPs was not an objective the overall difference in the perceived importance by time of diagnosis was similar for both physician groups.

This concept is supported by the fact that the physicians perceived the limitations in the same activities as comparable between patients with recent or longer diagnosis, even though they reported more patients with marked limitations in physical activity (CCS class 3) in the group with a longer diagnosis. In patients with coronary heart disease, Stewart et al. demonstrated that those with symptoms during exercise reported the least physical activity.[11](#_ENREF_11) Since exercise is an important part of the therapy for SA,[5](#_ENREF_5) a better understanding of the needs of patients with SA with regard to physical activity may help to improve the care for this population.

## Gender differences in clinical presentation and perception of stable angina

In the present survey, severity and frequency of angina was higher in women than in men (overall, and also for both cardiologists’ and GPs’ subsamples), possibly related to increased incidence of microvascular dysfunction in women[12](#_ENREF_12). Other studies using patient-directed questionnaires and GP clinical evaluations also showed that women with SA had more frequent angina,[2](#_ENREF_2), [13](#_ENREF_13) greater physical limitations and worse QoL than men.[13](#_ENREF_13) Even though a gender difference in SA severity and frequency was recognized and documented by the physicians in our survey, they perceived no difference between women and men when rating the patients’ current condition relative to their SA. This implies that physicians may underestimate perception of their female patients’ impaired QoL. As treatment decisions for SA are largely guided by physician assessment of the burden of angina, this could potentially lead to sub-optimal treatment in women.[2](#_ENREF_2), [6](#_ENREF_6)

We found that women were managed differently from men, with more frequent prescription of long-acting nitrates but less frequent use of beta-blockers, angiography, PCI and CABG. This different clinical management might reflect gender-related differences in pathophysiology, such as more prevalent microvascular dysfunction [12](#_ENREF_12) and less frequent obstructive coronary artery disease in women,[5](#_ENREF_5), [14](#_ENREF_14) which may preclude invasive management options in the treatment of SA, while data on the effectiveness of antianginal medications in women are limited.[15-17](#_ENREF_15) However, it is also possible that differences in clinical management may just reflect under-treatment in women, as seen in most areas of cardiovascular disease,[18](#_ENREF_18) perhaps because physicians might not accurately assess the impact of SA on women. There is ample evidence for gender disparities in diagnostic assessment and the use of evidence-based medical therapy for SA.[14](#_ENREF_14), [19](#_ENREF_19) This includes lower rate of revascularization and lower number of antianginal drugs in women,[19](#_ENREF_19) which is consistent with lower use of PCI and lower prescription rate for antianginal drugs in our survey.

Differences in clinical management may be explained in part by clinical factors,[14](#_ENREF_14) but gender-specific differences in the interaction with the physician, physician’s opinion, and gender-specific description and perception of symptoms, along with a lower perceived risk in women, may contribute.[19](#_ENREF_19) The more frequent presentation with symptoms other than angina in women, as shown in the present survey, might also lead to misdiagnosis and under-treatment.[14](#_ENREF_14) In young patients hospitalized with acute myocardial infarction, women were more likely to present with symptoms other than chest pain, and to perceive their symptoms as stress/anxiety compared with men. In patients who sought care before hospitalization, health care providers categorized women’s symptoms more often as not heart-related than in men.[20](#_ENREF_20) However, comparable treatment may not achieve the same results in men and women with SA. In the BARI-2D trial, where patients with diabetes and coronary artery disease were randomized to receive either optimal medical therapy or revascularization, women had more angina and poorer functional status than men throughout the 5-year follow-up period, despite very similar management and after adjustment for other factors.[21](#_ENREF_21)

Our findings are consistent with the literature, which reports worse clinical outcomes, lower QoL and less intensive therapy in women with SA. Thus, treatment strategies specifically targeted at women should be developed. In addition, new tools to improve communication between patients - both women and men - and physicians are warranted. One example is the STAR checklist,[22](#_ENREF_22) which could be easily applied to regularly assess angina severity and impact on QoL to guide treatment decisions, since available questionnaires such as the Seattle Angina Questionnaire[23](#_ENREF_23) and the Angina Plan[24](#_ENREF_24) are time-consuming for use in routine clinical practice.[22](#_ENREF_22)

## Medical management of stable angina after PCI

Almost half of the patients with SA in the present survey had a previous PCI; this percentage was significantly higher among patients reported by cardiologists than in those reported by GPs. Patients with PCI had more severe symptoms (more frequently CCS class 3) and longer duration of SA (3-5 years) than patients who never underwent PCI, suggesting that patients with PCI had more complicated and refractory SA. This group of patients was also more commonly followed by cardiologists, who have the full range of medical therapy available, which could explain greater use of beta-blockers, ranolazine, and ivabradine for angina treatment.

Overall, patients who continued to have or re-developed symptoms after PCI received more intense medical therapy but had more severe SA. PCI is guideline-recommended therapy for SA that is non-responsive to medical therapy.[5](#_ENREF_5) However, it has been shown that clinical benefits might be limited. The COURAGE trial on patients with chronic coronary artery disease did not show a reduced risk of death, myocardial infarction, or other major cardiovascular events during a median follow-up of 4.6 years when PCI as initial strategy was added to optimal medical therapy.[25](#_ENREF_25) A long-term follow-up for up to 15 years did not reveal any survival benefits either.[26](#_ENREF_26) Regarding angina burden and QoL, only temporary improvements were seen in that study.[27](#_ENREF_27) A higher proportion of patients in the PCI group were angina-free at 3 months; this difference was no longer present at 36 months. QoL based on the Seattle Angina Questionnaire yielded higher scores in the PCI group up to 24 months in the different domains. However, at 36 months differences between the groups were no longer statistically significant.

Our findings underline the importance of optimizing medical therapy, which is effective in patients with SA, to obtain the best possible angina control [28](#_ENREF_28). A different, more patient and symptom centered, more intensive and varied therapeutic approach including intensified risk factor management might be required for patients with SA after PCI.

***Limitations***

As with all surveys, our study has some inherent limitations. The responding physicians are those interested in participating. Therefore, the sample may not be representative of all physicians treating patients with SA, and the results may not entirely reflect clinical management seen in routine practice. Given its observational nature, our survey does not take into account every variable that could impact perceptions and SA management. In addition, the questionnaires were designed to cover specific aspects of interest, which limits the comparability with studies using standardized questionnaires.

# Conclusions

This survey shows that physicians (cardiologists and GPs) perceive the needs of patients with a recent or longer SA diagnosis differently, rating the importance of a variety of everyday activities as lower in patients living with SA for a longer time, even within homogeneous age groups. Physicians also appear to perceive and treat SA differently in men and women, whereby the impact of SA on the current condition for women was underestimated. Finally, physicians report that patients who still had angina after previous PCI had more severe SA and received more medical treatment than patients without PCI. Further studies comparing the perception of SA between patients and physicians could provide further insights into the needs of patients with SA and how these are met in clinical practice.

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Author contribution

All authors contributed to: (1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and, (3) final approval of the version to be published.

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The authors declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: GA has received consultation fees from Menarini International. PC has received honoraria from Berlin-Chemie, Menarini, Astra Zeneca, Bayer, Abbott and Ferris Pharmaceuticals. RD has received honoraria from Berlin-Chemie, Menarini, Servier, Bayer, MSD and Novartis. JLS has received honoraria for steering committee membership from AstraZeneca, Bayer, Boehringer Ingelheim, GlaxoSmithKline, Menarini, Merck, Novartis, Pfizer, Sanofi and Servier; honoraria for speaking from Amgen and Sanofi; and honoraria for consultancy from Boehringer Ingelheim and Menarini. AJM has received research grants from Sanofi, AMGEN and Bayer; and honoraria for lectures from Menarini, Ferrer, Servier and Recordati. AJC has received personal funds for acting as an advisor to Menarini.

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# References

1. Borras X, Garcia-Moll X, Gomez-Doblas JJ, Zapata A, Artigas R. Stable angina in Spain and its impact on quality of life. The AVANCE registry. Rev Esp Cardiol (Engl Ed). 2012;65:734-41.

2. Beltrame JF, Weekes AJ, Morgan C, Tavella R, Spertus JA. The prevalence of weekly angina among patients with chronic stable angina in primary care practices: The Coronary Artery Disease in General Practice (CADENCE) Study. Arch Intern Med. 2009;169:1491-9.

3. Fox K, Garcia MAA, Ardissino D, et al. Guidelines on the management of stable angina pectoris: executive summary. The Task Force on the Management of Stable Angina Pectoris of the European Society of Cardiology. Eur Heart J. 2006;27:1341-81.

4. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation. 2017;135:e146-e603.

5. Task Force Members, Montalescot G, Sechtem U, Achenbach S, et al. 2013 ESC guidelines on the management of stable coronary artery disease. The Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013;34:2949-3003.

6. Arnold SV, Grodzinsky A, Gosch KL, et al. Predictors of Physician Under-Recognition of Angina in Outpatients With Stable Coronary Artery Disease. Circ Cardiovasc Qual Outcomes. 2016;9:554-9.

7. European Pharmaceutical Market Research Association (EphMRA). Code of Conduct2017 2018-MAY-14 [cited 2018 May 14]. Available from: <https://www.ephmra.org/media/1044/ephmra-2017-code-of-conduct-october-2017.pdf>.

8. Rajendran S, Visvanathan R, Tavella R, et al. In patients with chronic stable angina, secondary prevention appears better in the very old compared to younger patients: the Coronary Artery Disease in gENeral practiCE (CADENCE) Substudy. Heart Lung Circ. 2013;wh22:116-121.

9. Al-Lamee R, Thompson D, Dehbi HM, et al. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial. Lancet. 2018;391:31-40.

10. Päivi M, Mirja H, Terttu P. Changes in Physical Activity Involvement and Attitude to Physical Activity in a 16-Year Follow-Up Study among the Elderly. J Aging Res. 2010;2010: Article ID 174290.

11. Stewart R, Held C, Brown R, et al. Physical activity in patients with stable coronary heart disease: an international perspective. Eur Heart J. 2013;34:3286-93.

12. Zuchi C, Tritto I, Ambrosio G. Angina pectoris in women: focus on microvascular disease. Int J Cardiol. 2013;163:132-40.

13. Dreyer R, Arstall M, Tavella R, et al. Gender differences in patients with stable angina attending primary care practices. Heart Lung Circ. 2011;20:452-9.

14. Kones R. Recent advances in the management of chronic stable angina I: approach to the patient, diagnosis, pathophysiology, risk stratification, and gender disparities. Vasc Health Risk Manag. 2010;6:635-6.

15. Bugiardini R, Bairey Merz CN. Angina with "normal" coronary arteries: a changing philosophy. JAMA. 2005;293:477-84.

16. Bairey Merz CN, Pepine CJ, Walsh MN, Fleg JL. Ischemia and No Obstructive Coronary Artery Disease (INOCA): Developing Evidence-Based Therapies and Research Agenda for the Next Decade. Circulation. 2017;135:1075-92.

17. Ambrosio G, Mugelli A, Lopez-Sendon JL, Tamargo J, Camm AJ. Management of stable angina: A commentary on the European Society of Cardiology guidelines. Eur J Prev Cardiol. 2016;23(13).

18. Wenger NK. Women and Coronary Heart Disease: A Century After Herrick. Understudied, Underdiagnosed, and Undertreated. Circulation. 2012;126:604-11.

19. Daly C, Clemens F, Lopez Sendon JL, et al. Gender Differences in the Management and Clinical Outcome of Stable Angina. Circulation. 2006;113:490-8.

20. Lichtman JH, Leifheit EC, Safdar B, et al. Sex Differences in the Presentation and Perception of Symptoms Among Young Patients With Myocardial Infarction: Evidence from the VIRGO Study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). Circulation. 2018;137:781-90.

21. Tamis-Holland JE, Lu J, Korytkowski M, et al. Sex differences in presentation and outcome among patients with type 2 diabetes and coronary artery disease treated with contemporary medical therapy with or without prompt revascularization: a report from the BARI 2D Trial (Bypass Angioplasty Revascularization Investigation 2 Diabetes). J Am Coll Cardiol. 2013;61:1767-76.

22. Camm AJ, Manolis A, Ambrosio G, et al. Unresolved issues in the management of chronic stable angina. Int J Cardiol. 2015;201:200-7.

23. Spertus JA, Jones P, McDonell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. Circulation. 2002;106:43-9.

24. Lewin RJ, Furze G, Robinson J, et al. A randomised controlled trial of a self-management plan for patients with newly diagnosed angina. Br J Gen Pract. 2002;52:194-6, 199-201.

25. Boden WE, O'Rourke RA, Teo KK, et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med. 2007;356:1503-16.

26. Sedlis SP, Hartigan PM, Teo KK, et al. Effect of PCI on Long-Term Survival in Patients with Stable Ischemic Heart Disease. N Engl J Med. 2015;373:1937-46.

27. Weintraub WS, Spertus JA, Kolm P, et al. Effect of PCI on quality of life in patients with stable coronary disease. N Engl J Med. 2008;359:677-87.

28. Manolis AJ, Poulimenos LE, Ambrosio G, et al. Medical treatment of stable angina: A tailored therapeutic approach. Int J Cardiol. 2016;220:445-53.

# Figure legends

### **Figure 1.** A) Importance of and B) limitations in everyday activities for patients with stable angina as perceived by physicians by duration of diagnosis.

\* Statistically significant difference between the two groups (t-test), p<0.05.

Survey question for importance: ‘In your opinion, to what degree does this patient consider it important to be able to perform the following activities? To answer, please choose a score from 1 (Not at all) to 5 (Extremely)’.

Survey question for limitations: ‘In your opinion, to what degree does stable angina limit this patient in performing the following activities? To answer, please choose a score from 1 (Not at all) to 5 (Extremely). To allow you to rate the items more precisely, the scale allows you to use also half points.’

For both questions, scores could be given from 1-5, with 0.5 fractions. The respondents could also answer, ‘Don’t know’.

### **Figure 2.** A) Symptoms of stable angina and B) number of angina attacks per month reported by men and women with stable angina according to the physicians’ perception.

SA, stable angina; SD, standard deviation.

\* Statistically significant difference between men and women (chi-square test), p<0.05.

Survey question for symptoms: ‘Symptoms of stable angina: Chest tightness / Heaviness, Chest pain, Breathing difficulties, Arrhythmia / Tachycardia, Fatigue, Arm pain, Strong sweat, Nausea / Vomiting, Dizziness, Stress / Anxiety / Depression, Jaw / Neck pain, Other (Specify)’ (No / Yes had to be selected for each item).

Survey question for number of angina attacks: ‘Number of reported angina attacks in a month (average number): Less than one, One, Two, Three, Four, Five-Seven, Eight-Ten, More than ten, Don’t know’.

### **Figure 3.** Current condition relative to stable angina in men and women as perceived by physicians.

No statistically significant differences between men and women were detected (chi-square test).

Survey question: ‘How would you define the patient’s current condition relative to his stable angina? Not good, Fair, Good, Very good’.

### **Figure 4.** Medical therapy in patients with stable angina with or without previous percutaneous coronary intervention

DHP, dihydropyridine; PCI, percutaneous coronary intervention.

\* Statistically significant difference between patients with stable angina with or without previous PCI (chi-square test), p<0.05.

Survey question: ‘Please enter the name of the product (or, if more than one, of the products) for SA in the current treatment of this patient, excluding other products that are not related with this disease.’