CARDIOVASCULAR COALITION
Joining Together for Patient Access

June 15, 2015

BY ELECTRONIC SUBMISSION

Maria Ellis
Executive Secretary for MEDCAC
Centers for Medicare & Medicaid Services
Center for Clinical Standards and Quality
Coverage and Analysis Group
S3–02–01
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Program; Meeting of the Medicare Evidence Development and Coverage Advisory Committee—July 22, 2015; [CMS–3320–N]

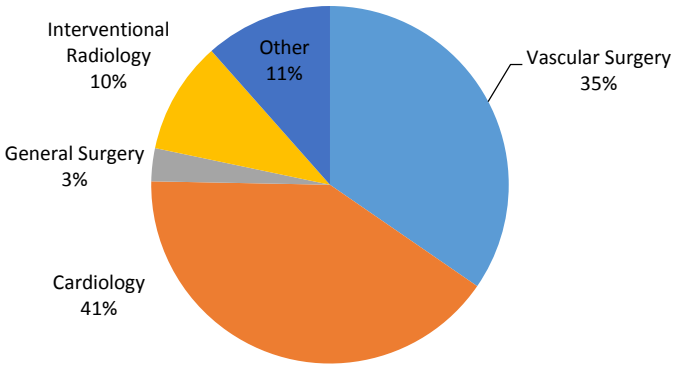
Dear Ms. Ellis:

The CardioVascular Coalition (CVC), appreciates the opportunity on behalf of physicians and staff in 26 states at over 149 freestanding centers where peripheral artery disease (PAD) services are performed to comment on the Centers for Medicare & Medicaid Services' (CMS) July 22, 2015 public meeting of the Medicare Evidence Development & Coverage Committee (MEDCAC). The CVC was established to provide policymakers and the public with a greater understanding of the value that non-facility providers of cardio/vascular interventions ("Freestanding Cardio/Vascular Centers", or "FCVCs") bring to their patients including the importance of logical, predictable payments to align incentives and ensure patient access to quality vascular care. CVC members include providers and manufacturers and CVC locations represent more than one-third of all FCVCs.[1]

Data show minimally invasive treatments for patients with PAD result in shorter hospital stays and have the potential to save Medicare millions of dollars each year. These treatments also can be done in FCVCs. Physicians, primarily trained in vascular surgery, cardiology, or interventional radiology treat nearly 113,000 Medicare fee-for-service patients at FCVCs.[2]

[1] For more information about the CVC, please see http://cardiovascularcoalition.com/about/
[2] Avalere Health, August 2014 analysis of CY 2012 Medicare claims

Figure 1: Physicians Who Practice at FCVCs



FCVCs offer a cost-efficient and focused alternative site of care for patients and focus on providing endovascular revascularization with minimally invasive techniques. In markets where an FCVC is available, more Medicare beneficiaries used the FCVC for their revascularization procedure. FCVCs are geographically located closer to patients and their communities, making quality vascular care more accessible and convenient for patients in need.

MEDCAC Panel Questions

The CMS meeting notice states that the purpose of this MEDCAC meeting is to "discuss lower extremity peripheral artery disease." Subsequent to the meeting notice, CMS posted a series of questions upon which the MEDCAC meeting panel will deliberate and vote. In this testimony, we will focus on the following issues relating to the questions posed to the MEDCAC panel:

- Amputation prevention, lower extremity PAD disparities and how they may affect the health outcomes of Medicare beneficiaries;
- Interventions that improve near-term and long-term outcomes of intermittent claudication and critical limb ischemia; and
- May 2013 AHRQ Comparative Effectiveness Review, "Treatment Strategies for Patients With Peripheral Artery Disease"

Amputation Prevention, Lower Extremity PAD Disparities and How They May Affect the Health Outcomes of Medicare Beneficiaries.

A key focus of the CVC is the utilization of appropriate vascular interventions to prevent non-traumatic amputations in patients. In the past decade, the global prevalence of Peripheral Artery Disease (PAD) increased by 24%, from 164 million to 202 million individuals[3], punctuating the need for increased intervention to properly treat PAD to halt progression of the disease. If untreated, PAD can lead to critical limb ischemia (CLI), a condition frequently associated with lower limb amputations.

[3] Fowkes, Gerald, The Lancet, "Comparison global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis." August 2013.

Data suggest that the increased use of vascular care procedures can be associated with lower rates of amputations. A recent study of more than 1 million Medicare patients with CLI found that proper intervention reduced the odds of amputation by 90%.[4] Increased access to interventions appears to have resulted in a reduction of lower extremity amputations for people with severe lower extremity PAD in the United States. From 1996 – 2011, the rate of lower limb amputations among Medicare patients in the US decreased by 45%, including a 48% decrease in the rate of above-knee amputations and a 39% decrease in the rate of below knee amputations.[5]

Lowering the incidence of non-traumatic amputations through clinically appropriate intervention has the potential to reduce healthcare spending, particularly Medicare expenditures. Major amputation is costly, ranking as the sixth most expensive surgical procedure in the U.S. The macroeconomic cost of amputation is estimated – at a minimum – at $10.6 billion annually.[6] Medicare is the largest payer of major amputations in the U.S., paying for 66% of procedures in 2010.[7]

Most importantly, interventions that ultimately result in limb preservation offer the best possible clinical outcome. When comparing patient amputees vs. those whose limbs were preserved, data show intervention produces positive results.

Limb Preservation[8]	Amputation[9]
The 2-year mortality rate is 16% to 24%	The one-year mortality rate for patients over 65 years old is 48% and the 3-year mortality rate is 71%
Almost two-thirds of patients are routinely discharged home	Only 18% to 24% of patients are routinely discharged home
Fewer than 20% of patients are discharged to a nursing home	A majority of patients (70%) go to another institution (a nursing home, rehabilitation facility)
At 2 years, 80% are walking and almost 90% are living independently	Sixty percent to 80% are unable to walk again
Data suggest patients who experience limb preservation have higher quality of life	One-third or more of patients experience depression, and in some, severe depression

Unfortunately, studies have shown that vascular diagnostics are underutilized notwithstanding "the proven benefit of revascularization in amputation-free survival and quality of life."[10] Vemulapalli et al. observed an overall arterial testing rate of 68.4% prior to amputation.[11] This included a rate of preamputation testing with ankle brachial indices (ABI) of only 47.5%

[4] Yost, Mary. Cost-Benefit Analysis of Critical Limb Ischemia in the Era of the ACA, May 2014.
[5] JAMA Surgery, Fifteen-Year Trends in Lower Limb Amputation, Revascularization, and Preventative Measures Among Medicare Patients, January 2015.
[6] Yost, Mary. Cost-Benefit Analysis of Critical Limb Ischemia in the Era of the ACA, May 2014.
[7] Yost ML. The economic cost of dysvascular amputation. Atlanta (GA): The Sage Group. In press.
[8] Yost, Mary. Cost-Benefit Analysis of Critical Limb Ischemia in the Era of the ACA, May 2014.
[9] Ibid
[10] Vemulapalli et al., Circ Cardiovasc Qual Outcomes. 2014; 7:142-150
[11] Ibid

(notwithstanding that PAD guidelines recommend ABI as part of the initial management of patients undergoing amputation), as well as angiography rates of only 38.7% (invasive angiography), 5.6% (MR angiography), and 6.7% (CT angiography) [12]

Perhaps as a result of this underutilization of vascular diagnostics, the CVC notes that there are still almost 43,000 Medicare patients per year receiving non-traumatic amputations with one-third of those patients receiving multiple amputations in the same year. [13] Medicare spending on CLI patients with major amputations averages $90,000, while Medicare spending on CLI patients who undergo revascularization and subsequently do not require an amputation is almost 40% less (around $58,000).[14] According to Avalere Health, policies that would encourage revascularization rather than a major amputation for Medicare patients could reduce Medicare spending by up to $2 billion over 10 years.[15]

Further underscoring this point, is the significant variation in care for CLI patients in Medicare. Specifically, revascularizations and amputations for CLI are performed by a wide range of providers, including vascular surgeons, cardiologists, interventional radiologists, general surgeons, and orthopedic surgeons as seen in the table below.[16]

% of all events with CLI diagnosis performed by specialty			
Specialty	Revascularization	Amputation, any	Other Care
Vascular Surgery	49.2%	17.6%	16.7%
Cardiology	15.7%	0.9%	7.3%
General Surgery	13.4%	15.8%	9.1%
Interventional Radiology	2.6%	0.0%	0.5%
Orthopedic Surgery	0.1%	13.2%	0.9%
Podiatry	0.0%	20.8%	15.1%

One area of further potential research relates to the extent to which patients served by these particular specialties have received vascular diagnostics before amputation. Some providers tend towards revascularization (interventional cardiologists and radiologists), others perform or are associated with a mix of revascularization and amputations (vascular surgeons and general surgeons), and others almost exclusively perform amputations (podiatrists and orthopedic surgeons). It is likely that more salutary clinical pathways towards amputation by a given specialty would be after a patient has been determined to be ineligible for revascularization as a result of vascular diagnostics. Policies that required vascular diagnostics to ensure a patient was not a candidate for revascularization before an amputation is performed could help to ensure variation in care for CLI patients by specialty is appropriate and not simply based on the type of physician the patient happens to be seeing at the time.

[12] Ibid
[13] Avalere Health, May 2015 analysis of CY 2011 – 2013 Medicare claims
[14] Ibid
[15] Ibid
[16] Avalere Health, June 2015 analysis of CY 2012 – 2013 Medicare claims

Interventions that Improve Near-Term and Long-Term Outcomes of Intermittent Claudication and Critical Limb Ischemia

The CVC supports randomized clinical trials (RCTs), comparative effectiveness trials, registries and other means of continuing to develop the evidence base relating to the complete spectrum of patients with PAD. Although medical therapy advances with antiplatelet, statins and antihypertensive agents have evolved significantly in terms of reducing CV major adverse events (MAE) of death, MI and stroke, these agents have not been demonstrated to improve QOL and CLI outcomes. Alternatively, endovascular device innovations and technology have allowed providers to treat an ever-expanding population of patients who were previously only candidates for medical therapy and conservative management. Unfortunately, patients treated through medical therapy or conservative management approaches often can progress to amputation or protracted and recurrent wound care.

With respect to the evidence base for endovascular devices, the AHRQ 2013 analysis is limited to studies published from 1995 to 2012 and predominately analyzes Percutaneous Transluminal Angioplasty (PTA) and bare metal stents as the primary endovascular revascularization modalities. However, several different atherectomy devices (including directional, orbital, rotational, excisional and laser atherectomy), drug eluting stents and drug coated balloons have been approved in the US since 1998 and such devices and techniques have evolved rapidly since 2006. Atherectomy is a therapeutic modality that preserves the native vessel for future treatment options without leaving a permanent implant (metal stent) behind. Atherectomy was developed as a therapeutic option to reduce the need for costly revision of in-stent restenosis, avoid/reduce the amount of barotrauma to the vessel, and lower dissection rates compared to PTA, while reducing the rates of target lesion revascularization.

Until recently, there have been no established definitions or consensus of clinical trial endpoints for PAD endovascular trials. The Peripheral Academic Research Consortium (PARC) was constituted in 2011 to standardize PAD definitions for consistency in future PAD trials. A working group of National and International Regulatory bodies, academia, medical societies, and industry participated over several years culminating in a manuscript published in JACC in March of 2015 entitled, Evaluation and Treatment of Patients With Lower Extremity Peripheral Artery Disease: Consensus Definitions From Peripheral Academic Research Consortium (PARC)."[17] In addition to PARC's effort and success in defining common data elements, other public and private partnerships are now working on establishing methods of extracting common data elements from both registries and electronic health records to help answer questions on PAD based on real world patients, not just the few and limited number of patients treated in clinical trials.

In addition to the aforementioned, the CVC would highlight the following more recent studies as additions to the evidence base:

- The DEFINITIVE LE study was one of the largest, prospective, multi-center studies, that included 800 patients and demonstrated that directional atherectomy is safe and effective

[17] Patel et al., J Am Coll Cardiol. 2015;65(9):931-941

(78% overall primary patency, 95% prevention of major amputation in CLI pts) in a variety of lesions, in patients with and without diabetes, and in claudicants and CLI patients. For intermittent claudication (IC) patients it showed significant improvement in Rutherford Scores from Rutherford 3.1 to 1.3 after one year. Additionally, Walking Improvement Questionnaire (WIQ) scores improved on all measures with improved pain, distance, speed and stair climbing after one year following atherectomy for IC. Also, the EQ-5D index and VAS scores significantly improved after 1 year following atherectomy. An important finding in this study was that the diabetic subgroups showed the similar patency rates compared to nondiabetics.[18]

- The CLEVER trial was a multicenter randomized study of 111 moderate to severe intermittent claudication patients with aortoiliac disease. It showed functional improvement favoring the supervised-exercise (SE) group but QOL improvement (WIQ, PAQ) favoring the endovascular (EV) stent group. Combined EV and supervised exercise showed improvement over optimum medical care (OMC) therapy alone at 6 mos.[19] At an 18 month follow up study, both functional status (peak walking times and claudication onset times) and QOL were better for the stent and SE groups compared to the OMC. This study was limited in that only aortoiliac lesions were enrolled and the femoral and infrainguinal anatomy was not known.[20]

- The EXCITE ISR trial which included 250 Rutherford 1-4 patients demonstrated a significant 52% reduction in TLR favoring excimer laser atherectomy (ELA) plus PTA over PTA alone for femoropopliteal ISR in a randomized, controlled, multicenter trial for long lesions which included CTOs (mean length 19.6 cm and 30.5% CTOs for ELA/PTA arm). Safety outcomes of MAE (death, amputation or TLR) significantly favored ELA plus PTA (5.8%) vs. PTA (20.5%) at 30 days.[21]

- The Zilver PTX was a randomized, prospective trial of 479 patients comparing the paclitaxel drug eluting stent (DES) with optimal PTA and BMS and showed primary patency of 74.8% and freedom from TLR of 60.8% at 2 years with presented 5 year data showing sustained benefit. Additionally, Rutherford class improved from 81.1% having > class 3 at baseline to 60.9% less than Rutherford class 1 after 2 years in the DES group. ABIs and WIQs were also significantly improved. [22]

- The In.PACT SFA was a prospective, randomized, multicenter, single-blinded study of 331 Rutherford 2-4 (IC and CLI) patients with femoropopliteal lesions comparing DCB to PTA in a 2:1 random assignment. It showed a very low rate of clinically driven TLR (CD TLR) of 2.4% in the DCB group compared to 20.6% in the PTA. It also showed higher primary patency results of the DCB vs. PTA arms for these femoropopliteal de novo lesions of 82.2% and 52.4%, respectively. Additionally, primary safety endpoints of device or procedure related deaths, clinically driven total vessel revascularization (CD

[18] McKinsey et al., JACC Cardiovasc Interv. 2014; 7(8):923-33
[19] Murphy et al., Circulation. 2012; 125(1):130-9
[20] Murphy et al., J Am Coll Cardiol. 2015; 65(10):999-1009
[21] Dippel et al., J Am Coll Cardiol Intv. 2015;8(1_PA):92-101
[22] Dake, et al., JACC. 2013;62(7):666

TVR) and target limb major amputation demonstrated safety (no deaths or amputations in either group). Major adverse events (MAE) defined as all- cause death, CD TVR, target limb amputation and thrombosis also were measured and confirmed safety of the DCB. Subgroup analysis of diabetics, long lesion length, chronic occlusions and gender also favored DCB over PTA. [23]

- The CALCIUM 360 trial was a 1:1 randomized, prospective, multicenter pilot study assessing the acute and long-term (12 months) results of orbital atherectomy (OA) + balloon angioplasty (BA) vs. BA alone. The trial included 50 patients with 64 below the knee (BTK) calcified lesions. The study found debulking with orbital atherectomy appeared to increase the chance of reaching a desirable angioplasty result, with less acute need for bailout stenting and a higher procedural success.[24]

- COMPLIANCE 360 trial was a 1:1 randomized, prospective, multicenter pilot study assessing the acute and long-term (12 months) results of OA + BA vs. BA alone. The trial included 50 patients with 65 above the knee (ATK) calcified lesions. The study found compared to BA alone, OA plus BA yields better luminal gain by improving lesion compliance and decreases adjunctive stenting in the treatment of calcified FP disease. At 12 months, the occurrence of TLR or restenosis was similar in both groups despite the large disparity in stent usage at the time of initial treatment.[25]

May 2013 AHRQ Comparative Effectiveness Review, "Treatment Strategies for Patients With Peripheral Artery Disease"

The 2013 AHRQ Comparative Effectiveness Review offers the following conclusions with respect to peripheral artery disease:

- Data is limited in the PAD space in general and CLI specifically for a multitude of reasons;
- More data is required on recent medical and invasive therapies;
- Antiplatelet therapy has mixed results with PAD patients;
- IC patients had improved functional status and QOL with various treatment modalities; and
- No differences in mortality or limb outcomes are apparent in endovascular or surgical revascularization but this is based on only one trial.

Since the AHRQ report was published in 2013 and based on clinical data available up to mid-2012, it does not include several publications which may help to address questions the MEDCAC panel will be considering. Some of those clinical publications are addressed in our testimony. In addition to those more recent manuscripts, there are several current and pending clinical trials which will add more evidence to the questions the MEDCAC is considering.

These new and pending trials are listed below with a brief synopsis of each trial.

[23] Tepe, et al., Circulation. 2015; 131 (5): 495-502
[24] Shammas et al., J Endovasc Ther. 2012;19(4):480-8
[25] Dattilo et al., J Invasive Cardiol. 2014;26(8):355-360

- The LIBERTY 360 observational study sponsored by Cardiovascular Systems Inc.
    - Up to 50 USA sites and 1,200 patients stratified by Claudication (Rutherford 2-3, n=500), CLI (Rutherford 4-5, n=600), and CLI (Rutherford 6, n = 100).
    - Study allows all endovascular technologies with virtually no inclusion / exclusion criteria. Patients will be followed for up to 3 years.
    - Prospective study and core lab adjudicated in the following areas: angiographic, duplex ultrasound, PPG, 6 min walk test, health economics.
    - Outcomes studied center include: procedural and lesion success, rate of major adverse events (includes amputation rates), duplex ultrasound / patency, quality of life (EQ-5d and VascuQOL), functional outcomes via six minute walk test, and economic outcomes.
    - First patient enrolled in mid-2013 and expected final enrollment in 2015. One year data presented in 2016, two year data in 2017, and three year data in 2018.

- The BEST trial sponsored by New England Research Institutes and funded in part by NIH.
    - Randomized prospective trial of BEST surgical interventions vs. BEST endovascular procedures in CLI patients who are eligible for both.
    - 2,100 patients will be studied for up to 50 months. Primary outcomes measured are time to major adverse event or death, whichever occurs first, in patients with or without surgery using Single Segment Great Saphenous Vein. Many secondary endpoints evaluated include major adverse events (including amputation), time to reintervention, quality of life, and treatment economics.
    - Inclusion / Exclusion criteria are significant and can be found on ClinicalTrials.gov.
    - Estimated enrollment completion in 2018 (from ClinicalTrials.Gov) would project one year data to be presented in 2019, two year data in 2020, and so on up to four year data in 2022 if the full four year follow-up is executed.

- The VIVA-BEST CLI (vCLI) Companion Registry sponsored by VIVA Physician Group
    - Registry developed due to the fact that most randomized clinical trials do not study "real world" patients. Due to rigid inclusion / exclusion criteria and inability to enroll potential patients even when they meet criteria, it is estimated that fewer than 15% of real world patients are ever studied in randomized trials.
    - The vCLI Companion Registry will focus on enrolling those patients who fail to meet the BEST trial inclusion / exclusion criteria.
    - While there are many aims to vCLI, the key assessments are: 1) identifying ratios of enrollment rates between BEST and vCLI and 2) the outcomes between the various primary and secondary endpoints in BEST and vCLI.
    - The BEST study leadership recently endorsed vCLI and enrollment of up to 5,000 patients is projected to begin in early 2016.

- The RAPID Project sponsored by the Medical Device Epidemiology Network (MDEpiNet) and the Predictable And SuStainable Implementation Of National Registries For Cardiovascular Devices (PASSION).
    - MDEpiNet and PASSION are public / private partnerships made up of: 1) global governmental regulatory and payor agencies, 2) academia, 3) medical societies, 4) patient advocacy organizations, and 5) industry.
    - RAPID (Registry Assessment of Peripheral Interventional Devices) is a three phased approach to gather the data needed on a prospective basis. Phase 1, projected to be completed in 2015, will standardize core data elements that could serve as a global case report form for both pre- and post-market assessment of peripheral interventional devices. Phase 2, projected to be completed in 2016, would involve implementation of these variables into at least 2 major existing US based registries (SVS VQI and ACC NCDR) and targeted electronic health records (EHR). The vision is international registries participate as well in the future. Phase 3, projected to be completed in 2017, would entail extraction of these variables from such registries and EHR systems, and using these to perform device evaluation projects with multi-sourced data.
    - RAPID is aligned with the current FDA initiative to improve total life cycle device surveillance. Peripheral interventional devices are produced by multiple manufacturers and used by multiple medical specialties, including cardiologists, radiologists and surgeons. Several society-based and industry-based registries have been developed to monitor these procedures, but there has been no attempt to standardize the core data elements necessary to evaluate devices across different registries or EHR systems.
    - Based on the RAPID project and the data it will generate over time in real world PAD patients treated with endovascular, surgical, medical and exercise therapy options, we can expect a significant increase in outcomes data for PAD patients.

- The In.PACT Global Trial sponsored by Medtronic Endovascular
    - 1500 pt. single arm, "real-world", prospective, core-lab adjudicated, and international trial comparing DCB to PTA for Rutherford 2-5 (IC and CLI) patients as well as long lesions, CTOs and de novo ISR cohorts.
    - Interim analysis of the first 655 patients show a low CD TLR rate of 8.7% at 1 year and target limb amputation rates of 0.3%.
    - Other safety endpoints of all cause death and thrombosis rates are low.
    - Estimated primary completion date of April 2016.

We believe the evidence derived from the aforementioned trials will add substantially to the current evidence base and allow for important updates to current practice guidelines based on clinical, quality of life and economic outcomes.

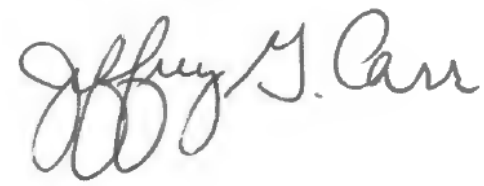
Conclusion

In sum, the CVC believes:

- Increased use of vascular care procedures can be associated with lower rates of amputations;
- Lowering the incidence of non-traumatic amputations through clinically appropriate intervention has the potential to reduce healthcare spending;
- Interventions that ultimately result in limb preservation offer the best possible clinical outcome;
- Vascular diagnostics are underutilized despite proven benefits of revascularization; and
- Patients with IC and CLI benefit from a comprehensive approach that can include risk factor modifications, exercise, and revascularization.

With respect to the current evidence base for such interventions, given the rapidly evolving and changing landscape of PAD, new and innovative technologies can render certain past data sets obsolete to guide current decision-making regarding indications and payment support for endovascular revascularizations. The CVC is committed to working with policymakers to continue to develop relevant comparative effectiveness data and evidenced-based decision making.

Sincerely,



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