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AT 12 MONTHS, BRILINTA PLUS ASPIRIN SIGNIFICANTLY REDUCED THE PRIMARY COMPOSITE END POINT of CV death, myocardial infarction (MI),† or stroke by 16% RRR (ARR 1.9%) vs clopidogrel plus aspirin.

The difference between treatments was driven by CV death and MI with no difference in stroke. *

BLEEDING AT 12 MONTHS, there was no significant difference in Total Major Bleeding (which includes Fatal and Life-threatening bleeding) for BRILINTA plus aspirin vs clopidogrel plus aspirin (11.6% vs 11.2%). There was a somewhat greater risk of Non–coronary artery bypass graft surgery (CABG)-related Major plus Minor Bleeding for BRILINTA plus aspirin vs clopidogrel plus aspirin (8.7% vs 7.0%) and Non–CABG-related Major Bleeding (4.5% vs 3.8%), respectively. The PLATElet inhibition and patient Outcomes (PLATO) trial did not show an advantage for BRILINTA compared with clopidogrel for CABG-related Bleeding (Total Major 85.8% vs 86.9% and Fatal/Life-threatening 48.1% vs 47.9%, respectively). When antiplatelet therapy was stopped 5 days before CABG, Major Bleeding occurred in 75% of patients treated with BRILINTA and 79% of patients on clopidogrel. **

INDICATIONS FOR BRILINTA 90-MG TABLETS
BRILINTA is indicated to reduce the rate of thrombotic cardiovascular (CV) events in patients with acute coronary syndrome (ACS) (unstable angina, non-ST-elevation myocardial infarction, or ST-elevation myocardial infarction). BRILINTA has been shown to reduce the rate of a combined end point of CV death, myocardial infarction (MI), or stroke compared to clopidogrel. The difference between treatments was driven by CV death and MI with no difference in stroke. In patients treated with PCI, it also reduces the rate of stent thrombosis. BRILINTA has been studied in ACS in combination with aspirin. Maintenance doses of aspirin >100 mg decreased the effectiveness of BRILINTA. Avoid maintenance doses of aspirin >100 mg daily.

IMPORTANT SAFETY INFORMATION ABOUT BRILINTA
WARNING: (A) BLEEDING RISK, (B) ASPIRIN DOSE AND BRILINTA EFFECTIVENESS
A. BLEEDING RISK
• BRILINTA, like other antiplatelet agents, can cause significant, sometimes fatal, bleeding
• Do not use BRILINTA in patients with active pathological bleeding or a history of intracranial hemorrhage
• Do not start BRILINTA in patients planned to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue BRILINTA at least 5 days prior to any surgery

• Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures in the setting of BRILINTA
• If possible, manage bleeding without discontinuing BRILINTA.
• Premature discontinuation increases the risk of MI, stent thrombosis, and death in the setting of BRILINTA

B. ASPIRIN DOSE AND BRILINTA EFFECTIVENESS
• Maintenance doses of aspirin above 100 mg reduce the effectiveness of BRILINTA and should be avoided. After any initial dose, use with aspirin 75 mg - 100 mg per day

CONTRAINDICATIONS
• BRILINTA is contraindicated in patients with a history of intracranial hemorrhage and active pathological bleeding such as peptic ulcer or intracranial hemorrhage. BRILINTA is contraindicated in patients with severe hepatic impairment because of a probable increase in exposure; it has not been studied in these patients. Severe hepatic impairment increases the risk of bleeding because of reduced synthesis of coagulation proteins. BRILINTA is also contraindicated in patients with hypersensitivity (eg, angioedema) to ticagrelor or any component of the product

WARNINGS AND PRECAUTIONS
• Moderate Hepatic Impairment: Consider the risks and benefits of treatment, noting the probable increase in exposure to ticagrelor
Fatal/Life-threatening 48.1% vs 47.9%, respectively). When antiplatelet therapy was stopped 5 days before CABG, Major Bleeding trial did not show an advantage for BRILINTA compared with clopidogrel for CABG-related Bleeding (Total Major 85.8% vs 86.9% and artery bypass graft surgery (CABG)-related Major plus Minor Bleeding for BRILINTA plus aspirin vs clopidogrel plus aspirin (8.7% vs 11.6% vs 11.2%). There was a somewhat greater risk of Non–coronary myocardial infarction (MI), † or stroke by 16% RRR (ARR 1.9%) vs clopidogrel plus aspirin.

AT 12 MONTHS, BRILINTA PLUS ASPIRIN SIGNIFICANTLY REDUCED THE PRIMARY COMPOSITE END POINT of CV death, MI, and stroke. In patients treated with BRILINTA or clopidogrel, CV death secondary end point: relative risk reduction (RRR) with BRILINTA plus aspirin (90 mg twice daily) was 1.1% (95% CI, −0.5% to 2.7%) vs clopidogrel plus aspirin (85% CI, 0.0% to 2.6%) (p < 0.05).

At 12 months, minor bleeding occurred in 75% of patients treated with BRILINTA and 79% of patients on clopidogrel.‡

• Do not start BRILINTA in patients planned to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue BRILINTA at least 5 days prior to any surgery planned to minimize bleeding risk.
• Do not use BRILINTA in patients with active pathological bleeding or a history of intracranial hemorrhage.

BRILINTA has been studied in ACS in combination with aspirin. In the treatment of ACS (unstable angina, non–ST-elevation myocardial infarction, or ST-elevation myocardial infarction), BRILINTA has been shown to reduce the rate of a combined end point of CV death, MI, and stroke. In patients treated with aspirin, non–coronary MI, † or stroke by 16% RRR (ARR 1.9%) vs clopidogrel plus aspirin. In clinical studies, BRILINTA has been shown to increase the occurrence of Holter-detected bradyarrhythmias. PLATO excluded patients at increased risk of bradycardic events. Consider the risks and benefits of treatment.

ADVERSE REACTIONS
• The most commonly observed adverse reactions associated with the use of BRILINTA vs clopidogrel were Total Major Bleeding (11.6% vs 11.2%) and dyspnea (14% vs 8%).
• In clinical studies, BRILINTA has been shown to increase the occurrence of Holter-detected bradyarrhythmias. PLATO excluded patients at increased risk of bradycardic events. Consider the risks and benefits of treatment.

Please see Brief Summary of Prescribing Information, including Boxed WARNINGS, on the adjacent pages.

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The PLATO study compared BRILINTA (180-mg loading dose, 90 mg twice daily thereafter) and clopidogrel (300-mg to 600-mg loading dose, 75 mg daily thereafter) for the prevention of CV events in 18,624 patients with ACS (unstable angina, non–ST-elevation myocardial infarction, or ST-elevation myocardial infarction). Patients were treated for at least 6 months and up to 12 months. BRILINTA and clopidogrel were studied with aspirin and other standard therapies. Excluding silent MI, PLATO used the following bleeding severity categorization: Major Bleed—Fatal/Life threatening. Any one of the following: fatal, intracranial, intrapericardial bleed with cardiac tamponade, hypovolemic shock or severe hypotension due to bleeding and requiring pressors or surgery; clinically overt or apparent bleeding associated with a decrease in hemoglobin (Hb) of more than 5 g/dL; transfusion of 4 or more units (whole blood or packed red blood cells [PRBCs]) for bleeding. Major Bleed—Other. Any one of the following: significantly disabling (eg, intracranial with permanent vision loss); clinically overt or apparent bleeding associated with a decrease in Hb of 3 g/dL; transfusion of 2 to 3 units (whole blood or PRBCs) for bleeding. Minor Bleed. Requires medical intervention to stop or treat bleeding (eg, epistaxis requiring visit to medical facility for packing). Minimal Bleed. All others (eg, bruising, bleeding gums, oozing from injection sites, etc) not requiring intervention or treatment.

Reference: 1. BRILINTA Prescribing Information, AstraZeneca.
BRILINTA® (ticagrelor) tablets, for oral use

BRIEF SUMMARY of PRESCRIBING INFORMATION

For full prescribing information, see package insert.

INDICATIONS AND USAGE
Acute Coronary Syndromes

BRILINTA is indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS) who are at risk of recurrent ischemic events, particularly myocardial infarction (MI) or stroke, with or without PCI, as an adjunct to standard antiplatelet therapy. BRILINTA should be administered as soon as possible after PCI, if tolerated.

BRILINTA is contraindicated in patients with a history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population [see Warnings and Precautions (5.2) and Clinical Studies (14) in full Prescribing Information].

BRILINTA is contraindicated in patients with a history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population [see Warnings and Precautions (5.2) and Clinical Studies (14) in full Prescribing Information].

WARNINGS AND PRECAUTIONS

• Maintain dosen of aspirin above 100 mg to reduce the effectiveness of BRILINTA and should be avoided. After any initial dose, use with aspirin 75-100 mg per day [see Warnings and Precautions (5.2) and Clinical Studies (14) in full Prescribing Information].

• ASPIRIN DOSE AND BRILINTA EFFECTIVENESS
• Maintenance doses of aspirin above 100 mg to reduce the effectiveness of BRILINTA and should be avoided. After any initial dose, use with aspirin 75-100 mg per day [see Warnings and Precautions (5.2) and Clinical Studies (14) in full Prescribing Information].

• DISEASES AND DISABILITIES
Acute Coronary Syndromes
BRILINTA is a P2Y12, platelet inhibitor indicated to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome (ACS) who are at risk of recurrent ischemic events, particularly myocardial infarction (MI) or stroke, with or without PCI, as an adjunct to standard antiplatelet therapy. BRILINTA should be administered as soon as possible after PCI, if tolerated.

BRILINTA has been shown to reduce the rate of a combined endpoint of ischemic events, including myocardial infarction or stroke compared to clopidogrel. The difference between treatments was driven by CV death and MI with no difference in stroke. In patients treated with PCI, it also reduces the rate of death from hemorrhage [see Clinical Studies (14) in full Prescribing Information].

BRILINTA has been studied in ACS in combination with aspirin. Maintenance doses of aspirin above 100 mg decreased the effectiveness of BRILINTA. Avoid maintenance doses of aspirin above 100 mg daily [see Warnings and Precautions (5.2) and Clinical Studies (14) in full Prescribing Information].

DOSE AND ADMINISTRATION

Initial BRILINTA treatment with a 180 mg (two 90 mg tablet) loading dose and continue treatment with 90 mg twice daily. After the initial loading dose of aspirin (usually 325 mg), use BRILINTA with a daily maintenance dose of aspirin of 75-100 mg.

ACG patients who have received a loading dose of clopidogrel may be started on BRILINTA.

After the initial loading dose, use with aspirin 75-100 mg per day [see Warnings and Precautions (5.2) and Clinical Studies (14) in full Prescribing Information].

The mixture can also be administered via a nasogastric tube (CH8 or greater). It is important to flush the nasogastric tube through with water after administration of the mixture.

Severe Hepatic Impairment

When possible, discontinue BRILINTA five days prior to surgery. Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures or is at high risk for bleeding.

The risk of bleeding because of reduced synthesis of coagulation proteins is increased in patients with acute coronary syndrome (ACS) who are at risk of recurrent ischemic events, particularly myocardial infarction (MI) or stroke, with or without PCI, as an adjunct to standard antiplatelet therapy. BRILINTA should be administered as soon as possible after PCI, if tolerated.

BRILINTA is contraindicated in patients with a history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population [see Warnings and Precautions (5.2) and Clinical Studies (14) in full Prescribing Information].

BRILINTA is contraindicated in patients with a history of intracranial hemorrhage (ICH) because of a high risk of recurrent ICH in this population [see Warnings and Precautions (5.2) and Clinical Studies (14) in full Prescribing Information].

Severe Hepatic Impairment

Avoid interruption of BRILINTA treatment. If BRILINTA must be temporarily discontinued (e.g., to treat bleeding or for elective surgery), restart it as soon as possible. Discontinuation of BRILINTA will increase the risk of myocardial infarction, stent thrombosis, and death.

Strong inhibitors of Cytochrome CYP3A

Ticagrelor is metabolized by CYP3A4. Avoid use with strong CYP3A4 inhibitors, such as azole antifungals, dipeptidyl peptidase 4 (DPP4) inhibitors, macrolide antibiotics, certain protease inhibitors, and nelfinavir. Avoid concomitant use of strong inhibitors of CYP3A (e.g., rifampicin, ritonavir, and other protease inhibitors).

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WARNING: (A) BLEEDING RISK, (B) ASPIRIN DOSE AND BRILINTA EFFECTIVENESS
• As shown in Table 1, BRILINTA was associated with a somewhat greater risk of non-CABG-related bleeding compared to clopidogrel. In PLATO, 1584 patients underwent CABG surgery. The percentages of those patients who bled are shown in Table 2. Rates were very high but similar for BRILINTA and clopidogrel.

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Table 1 – Non-CABG related bleeding (WN/D)

<table>
<thead>
<tr>
<th></th>
<th>BRILINTA (N=223)</th>
<th>Clopidogrel (N=186)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (Major + Minor)</td>
<td>15.7%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Major</td>
<td>5.4%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Major+Life-Threatening</td>
<td>2.1%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Fatal</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

Annualized rates of bleeding are summarized in Table 1 below. About half of the bleeding events were in the first 30 days.

Figure 1 shows major bleeding events over time. Most events are early, at a time of coronary angiography, PCI, CABG, and other procedures, but the risk persists during later use of antiplatelet therapy.

Figure 1 – Kaplan-Meier estimate of time to first PLATO-defined ‘Major Major’ bleeding event

This figure shows the Kaplan-Meier estimate of time to first PLATO-defined ‘Major Major’ bleeding event in patients treated with BRILINTA or clopidogrel. The y-axis represents the percentage of patients who have not experienced a major bleeding event. The x-axis represents time in months from randomization. The survival estimate for patients treated with BRILINTA is shown by the solid line, and the survival estimate for patients treated with clopidogrel is shown by the dashed line. The log-rank test was used to compare the Kaplan-Meier survival curves for BRILINTA and clopidogrel. The p-value is 0.010, indicating a statistically significant difference between the two treatments.

Adverse reactions are discussed elsewhere in the labeling. Dyspnea (see Warnings and Precautions (5.4) in full Prescribing Information)

Figure 1 shows the Kaplan-Meier estimate of time to first PLATO-defined ‘Major Major’ bleeding event in patients treated with BRILINTA or clopidogrel. The y-axis represents the percentage of patients who have not experienced a major bleeding event. The x-axis represents time in months from randomization. The survival estimate for patients treated with BRILINTA is shown by the solid line, and the survival estimate for patients treated with clopidogrel is shown by the dashed line. The log-rank test was used to compare the Kaplan-Meier survival curves for BRILINTA and clopidogrel. The p-value is 0.010, indicating a statistically significant difference between the two treatments.
In PLATO, the rate of study drug discontinuation attributed to adverse reactions was 7.4% for BRILINTA and 5.4% for clopidogrel. Discontinued patients in the absence of a placebo control, whether these are drug related cannot be determined in most cases, except where they are more common on BRILINTA or clearly related to the drug’s pharmacologic effect [see Adverse Reactions (6.1)].

Table 2 – CABG bleeds (KM%)

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<td>Total major</td>
<td>10.4%</td>
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Although the platelet inhibitor effect of BRILINTA has a faster onset than clopidogrel in in vitro tests and BRILINTA is a reversibly binding P2Y12 inhibitor, PLATO did not show an advantage of BRILINTA compared to clopidogrel for CABG-related bleeding. When antiplatelet therapy was stopped 5 days before CABG, major bleeding occurred in 7.7% of BRILINTA treated patients and 7.9% on clopidogrel. No data exist with BRILINTA regarding a hemostatic benefit of platelet transfusions.

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PCSK9: It has LDL receptors in a serious bind

Recent discoveries show there’s an important new factor to consider. PCSK9 is a protein that promotes degradation of the LDL receptor within hepatocytes, thereby increasing plasma LDL-C levels. Amgen Cardiovascular is proud to be a leader in PCSK9 research and remains dedicated to deepening our understanding of the critical role it plays in cholesterol metabolism. PCSK9 means it’s time to discuss cholesterol differently.

Unite the cholesterol conversation at DiscoverPCSK9.com.

LDL = low-density lipoprotein; LDL-C = low-density lipoprotein cholesterol;
PCSK9 = proprotein convertase subtilisin/kexin type 9.


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Health Care and War

There is a series of documents called the Geneva Conventions that recognizes that, even in war, there has to be a limit on violence. Thus, rules were established to provide some protection for the wounded, prisoners of war and non-participating civilians. Since August of 2014, the Geneva Conventions principles have been in existence for 150 years. Within the Geneva Conventions are such principles that medical workers are not considered combatants and have the right to provide care to the wounded on either side of a conflict. Thus, military hospital in a war theater will receive casualties from both sides and provide care, and that has been the case with American field hospitals in war. Because I was an active member of the Navy Reserve in 1990, I was recalled to active duty to help staff a field hospital in Saudi Arabia south of Kuwait. The hospital was mainly established to care for American military personnel participating in the first Gulf War, and we all reviewed the Geneva Convention to be sure we were providing proper care to our own military members, but also to others who were either allies or enemy combatants. We lived by the rule that, as medical personnel, we were protected from attack, and that our use of medical weapons was permissible. Our use of nuclear weapons was prohibited. We were an important means of providing on-site medical care to civilians as well as military personnel. These hospitals are often initially supplied with the needed medications and other supplies with operating rooms and x-ray machines so that a reasonable level of care can be provided. When we set up our 500-bed field hospital in Saudi Arabia in 1991, we staffed it with 1,000 personnel that included physicians of various specialties, nurses, pharmacists, physicians assistants, corpsmen, food service and engineering personnel, so that a fully operational hospital could be located in an area of need. The challenge for any field hospital is to maintain a continuous flow of medical supplies, food, water, fuel, and whatever else is needed to maintain [operations].

The challenge for any field hospital is to maintain a continuous flow of medical supplies, food, water, fuel, and whatever else is needed to maintain [operations].
Sudden Cardiac Death
Post-PCI and Post-MI

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Discuss It.
Prevent It.

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SCDFacts.org

The majority of mortality in post-PCI patients with low EF occurs in the first 3 months.¹

The risk of SCD post-MI is highest during the first 30 days.²³

Post-MI patients with HF are at 4–6 times greater risk of SCD in the first 30 days after MI.²⁴

High-risk post-PCI patients experience significant mortality during recovery from revascularization.

1 in 5 post-PCI patients are at high risk of dying.⁶

1 in 10 high-risk post-PCI patients die, with about 60% of this mortality due to sudden cardiac death.⁶


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Number Check | #✓

**Mental Illness and Creativity: Linked?**

25%

Scientists reported in a recent issue of *Nature Neuroscience* that creativity and certain psychoses “share genetic roots,” reporting that individuals who worked in creative professions such as musicians, painters, writers, and dancers, were 25% more likely to carry the genetic variants that raised the risk for bipolar disorder and schizophrenia than professions defined as less creative, such as farmers, manual laborers, and salespeople.


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**Cars Before Docs**

54%

The percentage of men in a new survey who remembered the last time they saw the doctor (vs 81% who remembered the make and model of their first car). The survey (part of the Drive for Men’s Health initiative) included 927 male respondents over the age of 18.

Still Too Much Second-hand Smoke

The percentage of non-smoking women exposed to second-hand smoke in their places of employment, according to a study published in the American Journal of Public Health. Exposure decreased with increasing age, earnings, and education.


More is Better

The reduced risk of death for patients with all forms of hemorrhagic stroke who were treated at a comprehensive stroke center compared to a non-stroke center. Moreover, the study also showed a 36% reduction in death over 90 days for those patients transferred to a comprehensive centers within 24 hours of diagnosis.


Forget Me Not

The number of statin users matched with an equal sized, non-user cohort in new study published online in JAMA Internal Medicine. The study suggested that the use of statins is associated with an increased risk of developing acute memory loss within 30 days of initiation, but the same association was also observed with non-statin lipid-lowering drugs. The retrospective cohort study compared 482,543 statin users 482,532 matched non-users of lipid-lowering drugs, and 26,484 users of non-statin lipid-lowering drugs.


A Generous Heart

The amount recently donated by Sarah Ross Soter—a heart disease survivor—to fund the Ross Soter Center for Women’s Cardiovascular Research. Currently, it is estimated that 43 million American women suffer from heart disease. “The American Heart Association is so grateful for Sally’s commitment to improving women’s heart health and to correcting the disparities that so many women face when it comes to accessing the care they deserve,” American Heart Association CEO Nancy Brown said.

Source: America Heart Association news release. May 19, 2015.
Beyond Ablation: Novel Therapies Ahead for AF

David Callans, MD: “The problem with the autonomic hypothesis has been how to augment it. The initial way of doing that has been to do what electrophysiologist always do which is try to destroy something. [...] The outcomes data for that have not been overwhelmingly convincing. There have been some positive studies, but not enough to really get people thinking about it.”


Particulate Air Pollution and Carotid Artery Stenosis

Johnathan D. Newman, MD: “The fine particulate air pollution that we investigated is a common source of air pollution from combustion: from car engines, from smokestacks, from wood burning, etc. It’s both visible and invisible. It is a component of smog, along with a lot of other air pollutants.”


The ACC’s In-Training Examination

Douglas Drachman, MD: “Once upon a time, people could attend a learning program and just based on the dwell time (the number of months you spent in the program), you could become certified. There was a test you had to take and had to answer those questions accurately in order to pass [...] nowadays, as a program director(s) and a CV fellowship director(s), we are held accountable to make sure the learners can perform certain procedures, express a certain amount of medical knowledge and demonstrate certain medical skill sets.”


Unintended Consequences: Effect of Changes in Payment for Peripheral Vascular Interventions

Manesh Patel, MD: “One of the things Medicare did was to say [that] outpatient procedures would get a global payment if a revascularization procedure happened. And that global payment would be less than a hospitalized payment, hoping that if patients can get an outpatient procedure in a clinic setting that they may be able to be cared for in a more expedited fashion.”


The Working Wounded: Occupational Hazards for Interventionalists and Allied Staff

Mandeep Singh, MD: “As we are so committed to the welfare and upkeep of our patients, we sometimes forget that our own health is at risk. This study actually surfaces that problem. In the proposals we are putting forward to our administration is that the technicians and nursing staff also need some time off—maybe 1 day per week, they go out and do some non-cath-lab work.”


Downstream Effects of Changes to Reimbursement for PCI

Sunil Rao, MD (R); with Amit Navin Vora, MD: “There has been significant change in the way that we pay for PCI, and primarily it’s been the shift from inpatient reimbursement to outpatient reimbursement. And that’s interesting because that’s really hospital-level reimbursement, and a lot of physicians aren’t aware of the differences.”


Multimedia Highlights
From the CardioSource WorldNews YouTube Channel | Scan the QR code to watch the full video
Patient Focus

FOCUS ON: MEN’S HEALTH

Get CardioSmart About Men’s Health

June is Men’s Health Month. Statistics show that men tend to die at higher rates than women, with heart disease the leading cause of death for one in every four men. Given most risk factors for heart disease and stroke—specifically high blood pressure, high cholesterol, smoking, and obesity—are preventable, there are clear opportunities for reversing this trend. For example, men’s health can be managed through the ABCS (appropriate Aspirin therapy, Blood pressure control, Cholesterol management and Smoking cessation). Encouraging men, along with their family members and other care providers, to follow through on annual examinations and preventive services is also key. Men are 100% less likely than women to visit the doctor for annual examinations and preventive services, according to the Centers for Disease Control and Prevention. Health care systems and providers can help men manage their heart health through use of electronic health records and data registries like the ACC’s PINNACLE Registry to identify, support and track progress of patients who need help quitting smoking or who have high blood pressure, diabetes or high cholesterol. Referring patients to community resources, such as quitting smoking and blood pressure self-management programs, or online sources like CardioSmart.org, can also play a huge role.

Cash Incentives Help Smokers Quit

A study conducted by researchers at the University of Pennsylvania and published in the New England Journal of Medicine compared four different employment-based smoking cessation programs that reward individuals for quitting smoking. Many employers, including CVS and General Electric, already offer programs to help their employees quit. Not only can these programs improve employee health and productivity, they may reduce company payouts to insurance companies. The question is: What’s the best type of smoking cessation program that employers can offer?

To learn more, researchers assigned more than 2,500 CVS employees to a variety of smoking cessation programs in 2012. Two programs simply rewarded smokers up to $800 for not smoking, while two others required a $150 deposit, which could be recouped only if smokers successfully quit. Each type of program had either an individual or group model, to see if one design worked better than the other. Some studies suggest that group programs make individuals more accountable, which could be useful when it comes to quitting smoking. Some participants were also assigned to standard education and counseling on smoking cessation, which offered no cash incentives.

After following participants for six months, researchers found that quit rates were much higher among those in cash incentive programs versus standard programming. Only 6% of smokers in the standard care group successfully quit after 6 months, compared to 9–16% of adults in the cash incentive programs. There was no difference in quit rates between the individual and group programs, suggesting that a sense of peer pressure or competition doesn’t increase smokers’ chances of quitting.

Interestingly, researchers also noted that subjects were much less likely to enroll in a smoking cessation program that requires a deposit. Of those assigned to the reward-based programs, 90% enrolled into the program. In comparison, only 14% of those assigned to the deposit-based programs actually enrolled.

Overall, findings suggest that adding cash incentives to smoking cessation programs dramatically increases smokers’ chances of quitting. However, rewards-based programs are much more appealing than deposit-based programs, which require smokers to risk their own money. This study suggests that adults are hesitant to put up their own money as part of a deposit program, especially when they risk losing it if they don’t successfully quit. Since deposits may create a barrier to enrollment, rewards-based programs may be the best way for employers to help smokers kick the habit and improve their health.
Obesity Increases Risk of AF

Incremental increases in body mass index (BMI) are significantly associated with an increased risk of incident, post-operative, and post-ablation atrial fibrillation (AF), according to a new study published May 27 in JACC: Clinical Electrophysiology.

Researchers examined data from a total of 51 studies including 626,603 participants. Studies were included if they were cross-sectional, case-control, or cohort studies that allowed for the assessment of associations between BMI and incident AF, post-operative AF, or post-ablation AF. For every five unit increase in BMI, there was a 19% to 29% greater risk of developing AF, a 10% greater excess risk of post-operative AF, and a 13% greater excess risk of recurrent AF post-ablation.

It is estimated that there are 33 million people living with AF worldwide. The annual incremental cost of AF is estimated at $26 billion in the United States, with hospitalizations—a major factor in cost—increasing faster than other cardiovascular conditions. As the population ages, this increase will further accelerate. The authors argue that a greater focus and effort is necessary to reduce the risk factors for AF in order to prevent its development and burden. Obesity is one of these risk factors, and may account for 60% of AF cases, as it is a modifiable risk factor that should be targeted to reduce the development of AF.

“The results of this study show that even moderate reductions in population BMI potentially could significantly reduce the burden of AF,” said Craig T. January, MD, PhD, writing committee chair of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial. “A decrease in obesity would also lower rates of conditions such as diabetes and hypertension, which are also risk factors for AF and would therefore have a greater impact on reducing this condition.”

Remnants of Residual Risk: Triglycerides Predict Recurrent Events

Among patients with acute coronary syndrome (ACS) treated effectively with statins, fasting triglycerides may predict long-term and short-term cardiovascular risk, according to a study published May 27 in JACC.

The study, based on analysis of patients in both the dal-OUTCOMES trial and the atorvastatin arm of the MIRACL (Myocardial Ischemia Reduction with Acute Cholesterol Lowering) trial, examined long-term and short-term relationships of triglycerides to risk after ACS. Analysis of dal-OUTCOMES included 15,817 patients (97% statin-treated) randomly assigned four to 12 weeks after ACS to either dalteparin or placebo and followed for a median 31 months. Analysis of MIRACL included 1,501 patients treated with atorvastatin 80 mg daily beginning 1 to 4 days after ACS and followed for 16 weeks.

Overall results found fasting triglyceride levels were associated with both long-term and short-term risk after ACS. In the dal-OUTCOMES Trial, long-term risk increased across quintiles of baseline triglycerides and researchers noted no interaction of triglycerides and treatment assignment on the primary outcome. In the atorvastatin group of MIRACL, short-term risk increased across quintiles of baseline triglycerides, with a hazard ratio of 1.51 (95% confidence interval: 1.05 to 2.15) in highest/lowest tertiles (>195/≤135 mg/dl). According to the study authors, the relationships of triglycerides to risk was independent of low-density lipoprotein cholesterol in both studies.

“Despite a background of effective statin treatment, we found a strong, unfavorable relationship of fasting triglyceride levels to long-term and short-term prognosis after ACS,” study authors said. “The hazard associated with increasing triglycerides was nearly identical in univariate analysis and after adjustment for risk factors usually associated with triglyceride levels, including age, sex, hypertension, smoking, diabetes, HDL-C, and body mass index, as well as LDL-C.” This observation suggests that triglyceride-rich lipoproteins may have a causal relationship to risk after ACS.”

Moving forward, the authors note it remains uncertain whether triglyceride-rich lipoproteins should be a target of therapy after ACS “above and beyond” statin treatment. Future studies will need to specifically examine the efficacy of triglyceride-lowering interventions after ACS.

“The questions of whether residual risk for recurrent atherosclerotic cardiovascular disease can be attributed to remnant lipoproteins, and to what degree, carry significant potential therapeutic implications, said Parag H. Joshi, MD, MHS, and colleagues in an accompanying editorial comment. “With the rise in metabolic syndrome and resultant increases in remnants, lifestyle modifications take on even greater importance as part of a structured preventative program.”

SIMPLE SOLUTIONS.
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The ACC Quality Improvement for Institutions program gives health care institutions a comprehensive suite of cardiovascular registries and service solutions – supporting quality clinical care and improving patient outcomes.

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More Than a Remote Chance: Wireless Monitoring Saves Lives

Remote monitoring may improve the outcomes of patients with implantable devices, according to two studies recently published in JACC.

In the first study, researchers analyzed data from nine randomized controlled trials to compare clinical outcomes in patients with implantable cardioverter-defibrillators (ICDs) who underwent remote monitoring to ICD patients who received conventional in-office follow-up. Specifically, they sought to evaluate the impact of remote monitoring on mortality, hospitalization, unscheduled clinic visits, device shocks, atrial arrhythmia detection, and the time taken to clinical decision or clinical event detection.

A total of 6,469 patients were included in the analysis, 3,496 of whom underwent remote monitoring and 2,973 who had in-office follow-ups. The data showed similar outcomes between the two groups for all-cause and cardiovascular mortality, as well as hospitalizations. However, remote monitoring patients who received a daily verification of shock were reduced in remote monitoring patients (and providers) must use it.” The researchers also state that a “healthy-user effect” may be the cause of the association, meaning that patients who use remote monitoring are less sick and more compliant, or they may have a physician who is more up-to-date with clinical practice or clinical event detection.

The current results illustrate the critical impact of adherence,” said the authors, led by Niraj Varma, MD, PhD, from Cleveland Clinic. “In order to benefit from remote monitoring, patients (and providers) must use it.” The researchers also state that a “healthy-user effect” may be the cause of the association, meaning that patients who use remote monitoring are less sick and more compliant, or they may have a physician who is more up-to-date with recommended treatment.

In an editorial accompanying both studies, James V. Freeman, MD, MPH, and Leslie Saxon, MD, said the findings showing “that remote monitoring utilization remains poor in clinical practice suggests that efforts to change treatment patterns through more aggressive use of guideline recommendations and continuing medical education should be undertaken at this point. Additionally, research must be conducted to better understand patient- and physician-level impediments to adopting remote monitoring and methods to address these barriers.”

“These studies show that remote monitoring can positively impact the care of patients with implantable devices,” added Jodie L. Hurwitz, MD, chair of the ACC’s Electrophysiology Section Leadership Council. “Remote monitoring can facilitate better patient care by replacing the need for in-office visits and, as these findings show, improve the outcomes of the patients as well. It is important to expand training and development of this technology in order for physicians and their staff to utilize it fully.”


Indoor Air Purifiers May Help the Heart

Fine particulate matter air pollution has proven to be significantly associated with increased cardiopulmonary morbidity and mortality. However, new data published June 2 in JACC finds that reducing the amount of these particles indoors with air purifiers may have cardiopulmonary benefits.

In this randomized, double-blind crossover study, 35 healthy college students living in dormitories in Shanghai, China, were observed. The students were randomized into two groups alternating the use of true or sham air purifiers for 48 hours with a 2-week washout interval. The particulate matter concentration in the rooms with a true air purifier was 57% lower than the rooms with the sham purifier.

Indoor air purification led to a significant geometric decrease of several circulating inflammatory and thrombogenic biomarkers, including 17.5% in monocyte chemoattractant protein-1, 68.1% in interleukin-1b, 32.8% in myeloperoxidase, and 64.9% in soluble CD40 ligand. There was a 2.7% decrease in systolic blood pressure and a 4.8% decrease in diastolic blood pressure. Fractional exhaled nitrous oxide was reduced by 17%. There was also indication of improved—but not statistically significant—lung function.

China has one of the highest levels of ambient fine particulate matter in the world, contributing to an estimated 1.2 million deaths and a loss of 24 million healthy years. According to the study authors, short-term indoor air purification may have modest cardiovascular benefits for young, healthy adults exposed to severe particulate air pollution and hypothesize that greater benefits may be seen in more vulnerable populations such as young children or older adults. There is also potential for greater benefits over a longer period of time. They add that “the use of air purifiers offers ordinary citizens a feasible and affordable way to reduce exposure to hazardous air pollution in a highly polluted developing country, such as China, leading to significant public health benefits.”

In an accompanying editorial, Sanjay Rajagopalan, MD, and Robert D. Brook, MD, write that the improvement of outdoor air quality is needed to change the indoor air quality in the cities of China and India. “In the meantime, personalized behavioral and small-scale interventions to lower exposures (e.g., filters in homes and cars) may be needed in order to optimally protect citizens in these areas.”

HEART FAILURE PATIENTS FACE A POOR PROGNOSIS

Despite advances in our understanding of its pathophysiology and treatment, chronic heart failure continues to carry a significant risk of hospitalization and death. In fact:

- ≥24% of patients die within 1 year of diagnosis
- ~50% of patients die within 5 years of diagnosis

Additionally, landmark trials have shown that even mildly symptomatic patients (NYHA class II) are at high risk of heart failure hospitalization and cardiovascular death. Even more alarming, an analysis of 6 trials or registries comprising over 10,000 patients showed that 65% of all deaths among NYHA class II patients were due to sudden cardiac death.

SUSTAINED NEUROHORMONAL IMBALANCE CONTRIBUTES TO HEART FAILURE DISEASE PROGRESSION

One of the key factors that contributes to heart failure progression is neurohormonal imbalance. Sustained overactivation of the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system (SNS) contributes to myocardial damage and worsening heart function.

NATRIURETIC PEPTIDES COUNTER THE EFFECTS OF THE RAAS AND SNS

The natriuretic peptide system (NPS) is one of the most important counterregulatory systems activated in chronic heart failure. Natriuretic peptides and other compensatory mediators help counter the effects of the overactive RAAS and SNS. Neprilysin, a neutral endopeptidase, metabolizes natriuretic peptides. As heart failure progresses, however, the beneficial effects of the NPS are diminished.

Even patients with mild symptoms (NYHA class II) face a high risk of hospitalization and death.

THERE IS AN URGENT NEED TO IMPROVE PATIENT OUTCOMES

There are currently 5.7 million patients with heart failure in the United States, and this number is expected to increase to more than 8 million patients by 2030. As the role of the NPS in heart failure becomes more appreciated, it’s clear that a better understanding of the impact of neurohormonal imbalance in heart failure is needed.

Today, regardless of symptom severity, every heart failure patient continues to be at risk for hospitalization and death.

Learn more at RethinkHF.com.

Kim Eagle, MD, and the editors of ACC.org's Journal Scans, present relevant articles taken from various journals.

PINNACLE India Program Demonstrates Feasibility of Quality Improvement in Resource-Limited Countries

While the burden of cardiovascular disease (CVD) in India continues to grow, there are limited data available on the quality of outpatient care. There has also been an increase in risk factors for coronary artery disease (CAD), such as smoking, physical inactivity, unhealthy diets, along with low levels of awareness, treatment, and control of CAD risk factors. The number of cardiologists for the highly-populated country is low and busy practitioners are often too overwhelmed to report or attempt to improve the quality of cardiovascular care.

According to new research from the ACC's PINNACLE India Quality Improvement Program (PIQIP), it is possible to collect and study the quality of outpatient cardiovascular care in research-limited environments. The pilot study, published May 20 in the Journal of the American Heart Association, examines performance measures and outlines areas for further improvements in the delivery of cardiovascular care.

Researchers studied PIQIP data from 10 Indian cardiology outpatient departments (HOPDs) and 68,196 patients. Hypertension was the most prevalent CAD factor in 29.7% of patients, followed by diabetes (14.9%), tobacco use (7.6%) and dyslipidemia (6.5%). CAD was present in 14.8% of patients, HF in 4.0% patients, and AFib in 0.5% of patients. Aspirin (48.6%), clopidogrel (37.1%), and statin-based, lipid-lowering therapies (50.6%) were taken by CAD patients, while RAAS antagonists (61.9%) and beta-blockers (58.1%) were used by HF patients. Anticoagulants were taken by 37% of AFib patients.

The PIQIP data revealed a significant difference by sex among cardiovascular disease prevalence, with women comprising only 7% of patients with CAD and 3% of patients with HF. Additionally, the authors also found that a younger median age of the represented populations with CVD and a relatively lower prescription of evidence-based medications for CAD, HF, and AFib.

The study authors also report several challenges related to the implementation of the PIQIP. Most of the outpatient departments did not use electronic health records, outpatient record-keeping was mostly non-existent, and the system in place made it difficult to track patients from one visit to another. There was also reluctance from busy physicians to use the web-based tracking tool, and staff required repeated training for the software. The authors report that several strategies are being considered for the future, including a model that allows outpatient departments to become self-sufficient in data collection and reporting; enhanced data capture, including socioeconomic variables, medication contraindication, and laboratory values; and expansion of the program to other sites across India.

“This paper demonstrates the high potential for the American College of Cardiology and the PINNACLE Registry to partner with cardiologists and help them improve the quality of outpatient cardiovascular care across the globe,” said William Oetgen, MD, ACC executive vice president of science, education, and quality and one of the study authors. The PIQIP is the first cardiovascular disease care data-collection and reporting program implemented in India. This study demonstrates that it is feasible to study the quality of outpatient cardiovascular care in this and other countries with limited resources.


The Consequences of Medicare Fee Cuts on Imaging Practices

When the Centers for Medicare and Medicaid reduced fees for cardiology services in 2010, focusing particularly on those delivered in private practices, the ACC predicted that many offices would integrate with hospitals in response. A new analysis published in JAMA: Internal Medicine has examined the effects these cuts had on practices and costs of cardiovascular imaging services.

The authors analyzed data from medical claims made between 2007 and 2012. The sample included 806,266 Medicare beneficiaries from every state and 12,567,069 commercially insured individuals with a similar geographic distribution. They also measured cardiologist-hospital integration by calculating the share of volume billed by hospital outpatient departments (HOPD), focusing on three affected services—myocardial perfusion imaging (MPI), echocardiograms, and electrocardiograms. For all services, prices favored the HOPDs after 2010. The shares of volume in HOPDs also increased after that year. Growth in the HOPD share was 5.9%, 3.9%, and 2.7% per year faster after 2010 compared with growth before 2010 for MPI, echocardiograms, and electrocardiograms, respectively.

The volume of echocardiograms and electrocardiograms per beneficiary continued to increase after the fee cut, while that for MPI decreased slightly.

The researchers also point out that similar results were seen across all cardiovascular imaging and cardiovascular medicine services. There were also similar results seen in commercial populations, suggesting that integration was associated with comparable effects across payers.

Cardiologist integration from private practice to hospital accelerated after the fee cuts. This reflects the ACC's 2010 Practice Census, which found that 40% of cardiologists planned to integrate with hospitals due to fee cuts and another 13% were considering it.

“Hospital outpatient departments may be more expensive than office setting because of the costs of licensing requirements, ancillary services, maintaining standby capacity, and treating more complex patients,” said the authors. “However, if equivalent quality care could be delivered in the office, the case for paying the higher fee may be more difficult to justify. Ultimately, integration may offset savings that fee cuts were attended to achieve, both because facility-based fees are higher and because of higher prices due to market power.”

There has been increased attention being paid to equalize payments as recognition for payment disparities has grown. If fee cuts are leading to the hospital acquisition of practices, the payment gap may need to be narrowed in order to lead to less integration and, in turn, limit price increases.

In a related commentary, Ralph Brindis, MD, an ACC past-president, and Eugene Sherman, MD, chair of both the ACC's Advocacy Steering Committee and Political Action Committee, note that “the current health care delivery challenges and resultant changes to the practice landscape demand creative and workable solutions to meet the needs of new practice and models as well as help current private practitioners maintain viability while simultaneously promoting high value in health care delivery.” They add that, in particular, the overuse of unnecessary tests and procedures can be addressed by implementing payment models that encourage appropriate testing while discouraging inappropriate testing, rather than by decreasing reimbursement. They write that “physicians will need to assume leadership in new delivery systems and health care policy to encourage all specialties to practice cost-effective medicine.”

8.6 Renal Impairment
Renal clearance accounts for approximately 50% of the total clearance of edoxaban. Consequently, edoxaban blood levels are increased in patients with poor renal function compared to those with higher renal function. Reduce SAVAYSA dose to 30 mg once daily in patients with CrCL 15-50 mL/min. There are limited clinical data with SAVAYSA in patients with CrCL < 15 mL/min; SAVAYSA is therefore not recommended in these patients. Hemodialysis does not significantly contribute to SAVAYSA clearance [see Dosage and Administration (2.1, 2.2) and Clinical Pharmacology (12.3) in the full prescribing information].

As renal function improves and edoxaban blood levels decrease, the risk for ischemic stroke increases in patients with NVAF [see Indications and Usage (1.1), Dosage and Administration (2.1), and Clinical Studies (14.1) in the full prescribing information].

8.7 Hepatic Impairment
The use of SAVAYSA in patients with moderate or severe hepatic impairment (Child-Pugh B and C) is not recommended as these patients may have intrinsic coagulation abnormalities. No dose reduction is required in patients with mild hepatic impairment (Child-Pugh A) [see Clinical Pharmacology (12.3) in the full prescribing information].

8.8 Low Body Weight Consideration for Patients treated for DVT and/or PE
Based on the clinical experience from the Hokusai VTE study, reduce SAVAYSA dose to 30 mg in patients with body weight less than or equal to 60 kg [see Dosage and Administration (2.2) and Clinical Studies (14.2) in the full prescribing information].

10 OVERDOSAGE
A specific reversal agent for edoxaban is not available. Overdose of SAVAYSA increases the risk of bleeding.

The following are not expected to reverse the anticoagulant effects of edoxaban: protamine sulfate, vitamin K, and tranexamic acid.

Hemodialysis does not significantly contribute to edoxaban clearance [see Pharmacokinetics (12.3) in the full prescribing information].

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Advise patients of the following:
- they may bleed more easily, may bleed longer, or bruise more easily when treated with SAVAYSA
- to report any unusual bleeding immediately to their healthcare provider
- to take SAVAYSA exactly as prescribed
- to not discontinue SAVAYSA without talking to the healthcare provider who prescribed it
- to inform their healthcare providers that they are taking SAVAYSA before any surgery, medical, or dental procedure is scheduled
- to inform their healthcare providers and dentists if they plan to take, or are taking any prescription medications, over-the-counter drugs or herbal products
- to inform their healthcare provider immediately if they become pregnant or intend to become pregnant or are breastfeeding or intend to breastfeed during treatment with SAVAYSA
- that if a dose is missed, take SAVAYSA as soon as possible the same day, and resume the normal dosing schedule the following day. The dose should not be doubled to make up for a missing dose
- that if they are having neuraxial anesthesia or spinal puncture, advise patients to watch for signs and symptoms of spinal or epidural hematoma, such as back pain, tingling, numbness (especially in the lower limbs), muscle weakness, and stool or urine incontinence. If any of these symptoms occur, advise the patient to contact his or her physician immediately [see Boxed Warning].
A new drug, still called LCZ696, combines two blood pressure-lowering medications: one of the most widely used angiotensin II receptor blockers (valsartan) and an agent from a new class of drugs called an angiotensin receptor neprilysin inhibitor (ARNI) known as sacubitril. The ARNI raises the level of endogenous natriuretic peptides by preventing their enzymatic breakdown in chronic heart failure (HF) patients.

At the 2014 meeting of the European Society of Cardiology (ESC), investigators presented the results of PARADIGM-HF, which stands for Prospective Comparison of ARNI with ACE-I (angiotensin-converting enzyme inhibitor) to Determine Impact on Global Mortality and Morbidity in Heart Failure. A total of 8,442 patients with class II, III, or IV HF and an ejection fraction <40% were randomized to receive either the combo agent of LCZ696 (at a dose of 200 mg twice daily) or enalapril (at a dose of 10 mg twice daily), in addition to recommended therapy.

The primary outcome was a composite of death from cardiovascular (CV) causes or HF hospitalization, but the trial was designed to detect a difference in the rates of death from cardiovascular causes.

### TABLE PARADIGM-HF: Sample Measures of Nonfatal Worsening Heart Failure

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Enalapril (n = 4,212)</th>
<th>LCZ696 (n = 4,187)</th>
<th>Hazard Ratio (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Worsening HF leading to hospitalization</td>
<td>604 (14.3%)</td>
<td>520 (12.4%)</td>
<td>0.84 (0.74 – 0.94)</td>
<td>0.003</td>
</tr>
<tr>
<td>Emergency department visit for HF</td>
<td>150 (3.6%)</td>
<td>102 (2.4%)</td>
<td>0.66 (0.52 – 0.85)</td>
<td>0.001</td>
</tr>
<tr>
<td>Patients hospitalized for HF</td>
<td>658 (15.6%)</td>
<td>537 (12.8%)</td>
<td>0.79 (0.71 – 0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total number of hospitalizations for HF</td>
<td>1,079</td>
<td>851</td>
<td>0.77 (0.67 – 0.89)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of patients requiring intensive care</td>
<td>623</td>
<td>549</td>
<td>0.87 (0.78 – 0.98)</td>
<td>0.019</td>
</tr>
<tr>
<td>Patients hospitalized for CV reasons</td>
<td>1,344 (31.9%)</td>
<td>1,210 (28.9%)</td>
<td>0.88 (0.81 – 0.95)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI = confidence interval; CV = cardiovascular; HF = heart failure

After a median follow-up of 27 months—and after enrollment had been completed—the trial was stopped early due to an overwhelming benefit favoring LCZ696. At the time of study closure, the primary outcome had occurred in 914 patients (21.8%) in the LCZ696 group and 1,117 patients (26.5%) in the enalapril group (hazard ratio [HR] in the LCZ696 group: 0.80; 95% confidence interval [CI]: 0.73–0.87; p<0.001). This means the trial was stopped after reaching the clinical events deemed necessary for statistical significance: the study design estimated a need for 1,229 deaths from CV causes, to provide an 80% power to detect a relative reduction of 15% in the risk of death from CV causes. In point of fact, there had been a total of 1,251 such deaths when the pre-specified boundary for halting the trial had been crossed.

(Specifically, 891 [13.3%] LCZ696 and 693 [16.5%] enalapril patients died from CV causes [HR: 0.80; 95% CI: 0.71–0.89; p<0.001]. Results also showed that a total of 711 patients (17.0%) receiving LCZ696 versus 835 patients (19.8%) receiving enalapril died (HR for death from any cause: 0.84; 95% CI: 0.76–0.93; p<0.001). LCZ696 also reduced the risk of HF hospitalization by 21% (p<0.001) versus enalapril and decreased the symptoms and physical limitations of HF (p<0.001). The LCZ696 group had higher proportions of patients with hypertension and nonserious angioedema but lower proportions with renal impairment, hyperkalemia, and cough than the enalapril group.

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TOO GOOD TO BE TRUE?

Skepticism is healthy and was certainly evident after the trial’s presentation at ESC’14. Indeed, a recent paper with additional data was accompanied by an editorial simply titled, “LCZ696: Too Good to Be True?”. The author was Robert M. Califf, MD, Professor of Cardiology at Duke University, now on leave after being named the Food and Drug Administration (FDA) Deputy Commissioner for Medical Products and Tobacco. Missing from the PARADIGM-HF main results was the clinical impact of the novel intervention over the period of follow-up post-randomization. Some of those details have been subsequently published. In brief, compared with enalapril, patients on LCZ696 were less likely to:

- show symptomatic deterioration
- need intensification of oral therapy/addition of intravenous (IV) therapy
- visit the emergency department
- be admitted to the hospital
- go to the intensive care unit (ICU) when admitted and less likely to need IV therapy require devices/surgery for worsening/end-stage HF (although not statistically significant)
- die prematurely (either suddenly or from worsening HF)
- show biomarker evidence of cardiac wall-stress and myocyte injury.

In short, LCZ696 slows progression of HF, delaying/preventing nonfatal and fatal worsening. Also, benefits were consistent regardless of the baseline NYHA functional class.

There are still questions as to whether the effects seen in PARADIGM-HF will also be seen to the same extent outside of the clinical trial setting. There was a single-blind run-in period during which all patients received enalapril, followed by a single-blind run-in period during which all patients received LCZ696. This was done to ensure an acceptable side-effect profile of the study drugs at target doses. A total of 9,419 patients entered the roll-in period with 977 (10.4%) discontinuing study participation. While there were multiple reasons for patients not making it to randomization, not being able to tolerate the therapy was a factor. So it is not possible to know whether an individual patient will tolerate LCZ696 at the time of treatment initiation—and the key toxicities (hyperkalaemia and hypotension) tend to occur...
early and thus were screened out in the PARADIGM-HF run-in phase.

In another editorial comment accompanying some of these new data, Henry Krum, MBBS, PhD, Head of the Clinical Pharmacology Unit and Director of the Monash University (Australia) Centre of Cardiovascular Research and Education in Therapeutics, noted that in the real-world adverse events may very well occur with even greater frequency with LCZ696 and will require careful review during post-market surveillance should the drug be approved.7

There are still mechanistic issues that need to be worked out and PARADIGM-HF was not a mechanistic study, so it can’t explain why the new combination works so well. PARADIGM-HF, he said, should rather be viewed as a pragmatic study asking the question of whether the newer agent is clinically superior to current best practice management of systolic chronic HF patients. With the new data, Dr. Krum wrote, “LCZ696 clearly meets any and all reasonable criteria for clinical superiority versus conventional therapy.”

ALZHEIMER’S QUESTION

Finally, another issue was raised recently: could long-term use of this new drug increase the risk of Alzheimer’s disease?8 The issue revolves around the ability of LCZ696 to inhibit an enzyme that fights sticky plaques in the brain. The paper, published in the European Heart Journal, cautioned that previous studies suggest that an ARNI might accelerate progression of Alzheimer’s.

According to The Wall Street Journal (February 26, 2015), the question was enough for Novartis to amend one of its continuing trials of the drug to add measures of cognitive function to the trial. Trial investigators have also said that the drug might even improve cognitive function through increased blood flow.

How this plays out will be interesting. The Wall Street Journal noted that analysts see LCZ696 as a potential blockbuster that could generate as much as $5 billion in sales by 2020. The U.S. FDA granted priority review to the drug in February 2015, meaning the drug could be approved as early as August. Canada also has decided to expedite the drug’s review.

One thing is sure: we’ll be hearing a lot more about LCZ696—or whatever they ultimately decide to call it.

REFERENCES:


Is it Really Resistant Hypertension?

Often, the data suggest, it is not

Given the well-established increased CV risk associated with elevated blood pressure (BP), hypertension poses a growing challenge for health policy-makers and physicians worldwide. A high-tech approach to the problem recently stumbled with the results of Symplicity-III (HTN-3), the first blinded, randomized, multi-center study on the efficacy of renal denervation for the treatment of resistant hypertension. There was no significant reduction of BP in patients with resistant hypertension after renal-artery denervation (neither at 6 months or 3 years) compared with controls.1,2

Consequently, attention has refocused on drug therapy. Secondary forms of hypertension and associated conditions such as obesity, sleep apnea, and primary aldosteronism are common in patients with apparent treatment-resistant hypertension (tTRH). True, resistant hypertension is associated with a high risk of CV and renal events, so it’s important to identify patients with tTRH.

Roland E. Schmieder, MD, is a professor of internal medicine, nephrology and hypertension, and he is head of the Clinical Research Center of Hypertension and Vascular Medicine at the University Hospital, Erlangen, Germany. He emphasizes that uncontrolled hypertension is not synonymous with resistant hypertension. Patients with true treatment resistance comprise a much smaller share of the population of patients who lack BP control on treatment, including those on inadequate treatment regimens, those with poor adherence, and those with undetected secondary hypertension. He adds that before it can be declared aTRH, “the treatment plan must include attention to lifestyle measures.”

Dr. Schmieder also noted that prognosis is “severe” in patients with aTRH: various studies suggest an all-cause death rate in these individuals of 2% to 4% per year and a major adverse cardiac and cerebrovascular event rate of 4% to 6% per year.

DEFINITION AND INCIDENCE

There are some variations in the definition of aTRH, but the core definition seems to be: failure to reach BP goal in patients who are adhering to full doses or “optimal” doses of an appropriate three-drug regimen that includes a diuretic.

The most detailed definition comes from Europe: aTRH occurs when appropriate lifestyle measures plus a diuretic and two other antihypertensive drugs belonging to different classes at adequate doses (but not necessarily including a mineralocorticoid receptor [MR] antagonist) fails to lower systolic (SBP) and diastolic (DBP) values to <140 and <90 mm Hg, respectively.3

Depending on the population examined and the level of medical screening, the prevalence of aTRH ranges from 5% to 30% of the overall hypertensive population, with estimates of <10% probably representing the true prevalence.

In the U.S., one often-cited estimate comes from the National Health and Nutrition Examination Survey (NHANES) from 2003 through 2008. Published in 2011,4 the analysis covered nonpregnant adults with hypertension whom were classified as resistant if their blood pressure was ≥140/90 mm Hg and they reported using antihypertensive medications from three different drug classes or drugs from ≥4 antihypertensive drug classes regardless of blood pressure. The NHANES data indicated that 8.9% of U.S. adults with hypertension met the criteria for resistant hypertension, which translated to 12.8% of the antihypertensive drug-treated population. These figures suggest an increasing number of the U.S. population has treatment resistant hypertension, based on 1988-1994 and 1999-2004 NHANES data (p<0.01 for trend across these time periods versus 2005-2008).

Two aspects to stress regarding the NHANES data:

1. Most (85.6%) of the individuals with resistant hypertension used a diuretic. Still, 15% did not; that’s important given that most definitions of true resistance indicate that one of the trio of drugs used should be a diuretic.
2. Of this group on diuretic therapy, 64.4% used the relatively weak thiazide diuretic hydrochlorothiazide. Again, if the definition requires optimization of antihypertensive therapy, then some of these NHANES patients considered ‘resistant’ might actually fail the actual definition.

The NHANES data suggest some clinical determinants of resistant hypertension (all p<0.001): these individuals were all more likely to have albuminuria, reduced renal function, and self-reported medical histories of coronary heart disease, HF, stroke, and DM.

ATRH: IS IT REALLY WHAT IT SEEMS?

Let’s face it: secondary causes and other ‘issues’ are often missed in patients wherein resistant hypertension seems to be the problem. Verloop and colleagues from the Netherlands found a sizable number of patients referred for renal denervation who had secondary causes of hypertension that had been missed or other problems that argue against intervention.5

At the University Medical Center, Utrecht, Netherlands, for example, patients referred...
Diabetes and Coronary Artery Disease: Is PCI still an option? 20 years after BARI, is there reason to believe it's different now?

Patients with diabetes mellitus (DM) are prone to a diffuse and rapidly progressive form of atherosclerosis, which increases their likelihood of requiring revascularization. So, it should be no surprise that 30% to 35% of patients undergoing revascularization have DM.1 Presence of diabetes is associated with worse outcomes for both coronary intervention and bypass surgery and, even since publication of the BARI (Bypass Angioplasty Revascularization Investigation) study,2 it has been thought that CABG is better than PCI for patients with DM and multi-vessel disease.

Is that still true? Many advances have occurred in the nearly 20 years since publication of the BARI results. Drug-eluting stents (DES), for example, are broadly used and the second-generation devices significantly reduce restenosis rates in patients with and without DM compared with bare-metal stents (BMS). In recent years, papers have shown conflicting results in terms of whether PCI remains a correlate of restenosis in patients with DM.

Recently, Stone and colleagues conducted an analysis of 18 pooled randomized trials to assess whether baseline lesion complexity affects outcomes following PCI with DES according to diabetic status.3 The study, the largest analysis to date examining DES outcomes relating to DM, suggested that freedom from repeat revascularization 1 year post-DES was comparable in patients with and without diabetes at least for simple stented lesions (TABLE). However, for patients with diabetes and complex lesions, there were significantly higher rates of repeat revascularization after DES than individuals without DM.

We also now have 5-year results from the Syn- tax (Synergy Between PCI with TAXUS and Cardiac Surgery) trial of patients with 3-vessel disease...
“There are clearly tradeoffs between the two revascularization strategies that need to be discussed with patients as part of the shared decision-making process.”

- Robert A. Harrington, MD

treated with CABG or PCI. The results suggest that CABG should remain the standard of care for patients with diabetes as this approach resulted in significantly lower rates of death, MI, and repeat revascularization than PCI, while stroke rates were similar. One issue that could affect the trial results: the comparator to CABG was first-generation paclitaxel-eluting stents (PES).

GENERATION GAP?
The aforementioned analysis by Stone and colleagues included studies of both first- and second-generation DES and was not powered to examine the impact different types of DES might have had on the interaction between DM status and lesion complexity. However, stent type was used as a variable for the propensity score match to minimize the impact of any such effects.

In this regard, although a network meta-analysis of randomized trials suggested that everolimus-eluting stents might be the safest and most efficacious in patients with DM, a recent nationwide study did not show substantial differences in clinical restenosis rates between different stent types in patients with DM. Use of EES was associated with improved outcomes compared with sirolimus-eluting stents (SES) or PES, mainly driven by lower rates of stent thrombosis and mortality. These results suggest better safety rather than efficacy with EES when compared with first-generation SES or PES.

The SYNTAX trial authors acknowledged that patients with complex CAD (intermediate or high SYNTAX scores) particularly benefit from CABG, whereas PCI is an acceptable treatment option in patients with less complex disease (low SYNTAX scores) particularly benefit from CABG, but PCI was associated with a higher risk of MI (among patients with incomplete revascularization) and repeat revascularization but a lower risk of stroke.

In the Future Revascularization Evaluation in Patients with Multivessel Disease (FREEDOM) trial, the SYNTAX trial authors acknowledged that patients with complex CAD (intermediate or high SYNTAX scores) particularly benefit from CABG, whereas PCI is an acceptable treatment option in patients with less complex disease (low SYNTAX scores), though at a price of significantly higher rates of repeat revascularization.

In direct comparisons, CABG has been shown to be associated with fewer repeat revascularizations than PCI, but questions have been raised about incremental improvements in stent technologies that might narrow the outcome gap between these two approaches.

When comparing patients with and without diabetes, the data suggest tradeoffs between these two revascularization strategies that need to be discussed with patients as part of the shared decision-making process.

Also, there is a need for better ways to aggregate and analyze large amounts of clinical data to better inform practice at the point of care.

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THE IMPACT of
CLIMATE CHANGE,
POLLUTION,
and WAR
ON MEDICINE

FUTURE CV SHOCK

by Debra L. Beck
When one thinks about the future of cardiovascular medicine, the mind may wander in different directions. For some, the path is new drugs, enhanced imaging, and even novel ways of testing new therapies, all coalescing to improve patient outcomes.

For others, the thought process flows another way and the future is less cheery: increasing pollution will have adverse effects on cardiovascular health, global warming will cause new problems as well as a resurgence of old health problems, and increasing numbers of people and countries will be torn apart by conflict, hardly able to access any medical care much less cardiovascular care. The planning committee for the 2015 American College of Cardiology (ACC) Scientific Sessions, as part of a new 13-session track devoted to the future of cardiovascular medicine, traveled this darker road and came up with a decidedly apocalyptic list of near-future woes affecting global cardiovascular health: climate change, pollution, and whole countries ripped asunder by war.

The session was designed to promote greater awareness that having to wait for an MRI for your patient may not be the worst thing to ruin a workday. “There is a lot going on around us, outside our normal cardiovascular science, that affects the cardiovascular health of our nation and our world,” said Ralph G. Brindis, MD, MPH, from the University of California, San Francisco, who led the session entitled: Beyond Medicine - Impact of Climate Change, Pollution, Population Migration, War: Future of Cardiovascular Medicine XIII.

In an ACCEL interview, session panelist William A. Zoghbi, MD, fromMethodist DeBakey Heart Center and Houston Methodist Hospital (Texas), added, “The topic is unusual and I’m glad the ACC chose to highlight it because I think there are some developments here...Let’s think globally a bit.”

“As cardiologists, we are going to be looking well beyond blood pressure and cholesterol as we look at the way the world around us is changing, and certainly when you add to that the trauma and the problems we’re seeing with current conflicts around the world, there is more than enough for those of us that are interested in international work,” noted panelist Sidney C. Smith, Jr., MD, from the University of North Carolina, Chapel Hill.

Add in Salim Yusuf, MD, DPhil, from McMaster University, Hamilton, Ontario, Canada, and the session panel was a veritable who’s who of CV medicine leadership.

So what do these experts say lies ahead around the globe?

**Warming Up to Climate Change**

Whether due to natural forces or the influence of human activities, climate change is happening. A report from the U.S. National Institute of Environmental Health Sciences (NIEHS) notes that the environmental consequences of climate change, including those already observed and those anticipated—such as sea-level rise, changes in precipitation resulting in flooding and drought, heat waves, more intense hurricanes and storms, and degraded air quality—will affect human health both directly and indirectly.1

Some confusion reigns in regard to the difference between climate change and weather patterns. The latter describe short-term events, while climate change is a longer process that affects the weather. Record-breaking cold and heavy rain and snow conditions, such have been experienced in much of North America, are actually consistent with global warming as an overall warmer planet changes weather patterns throughout the year everywhere.

Several cardiovascular diseases (CVD) show climate sensitivities, with both extreme cold and extreme heat directly affecting the incidence of hospital admission for chest pain, acute coronary syndrome, stroke, and variations in cardiac dysrhythmias. Such weather conditions serve as stressors in individuals with pre-existing CVD and can directly precipitate exacerbations. For example, the stress of specific events, and anxiety over event recurrence, are associated with myocardial infarction, sudden cardiac death, and the development of stress-related cardiomyopathy.

Climate itself also stands as an indirect risk for CVD: the incidence of certain vector-borne and zoonotic diseases impacts cardiovascular manifestations. Some occur predominantly outside the U.S., such as Chagas disease, which is an important cause of stroke and heart failure in Latin America (but not in the United States). On the other hand, Lyme disease is a prevalent vector-borne disease in the U.S. that has cardiovascular manifestations.

While there is little published literature projecting direct and indirect impact of climate change on CVD incidence, the NIEHS notes that insofar as climate change will bring increased ambient temperatures, increasingly variable weather, and increased extreme events, “we can infer that climate change will likely have an overall adverse impact on the incidence of cardiovascular disease.”

**Air Pollution: A Breath of Not-so-fresh Air**

Numerous studies have linked exposure to fine particle pollution to a variety of health problems including increased respiratory symptoms (irritation of the airways, coughing, difficulty breathing), decreased lung function, aggravated asthma, development of chronic bronchitis, arrhythmias, nonfatal heart attacks, and premature death in people with heart or lung disease.

A 2010 American Heart Association (AHA) Scientific Statement on the topic concluded that particulate matter (PM) is a “causal factor” in both the development of atherosclerosis and the triggering of CVD-related mortality and nonfatal events.

“It comes in many different packages, whether it’s a coal refinery north of Beijing or an indoor stove in India. This is a contributor to the development of atherosclerotic vascular disease,” said Sidney C. Smith Jr., MD, one of the authors of the 2010 AHA statement.

Importantly, the AHA statement also said that “reductions in PM levels are associated with decreases in cardiovascular mortality within a time frame as short as a few years.” Dr. Smith noted that there have been successful efforts to reduce exposure to second hand smoke, with attendant
WHO: Pollution Produces 7 Million Premature Deaths

In 2014, the World Health Organization (WHO) released new estimates that suggested that in 2012 around 7 million people died—one in eight of total global deaths—as a result of air pollution exposure. This figure was more than double previous estimates, confirming that air pollution is now a leading environmental health risk.

What was particularly surprising about the data: a much stronger link emerged between both indoor and outdoor air pollution exposure and cardiovascular diseases, including stroke. Indeed, the WHO stated that about 40% of outdoor air pollution-related deaths were attributable to ischemic heart disease, and another 40% to stroke. As for indoor pollution-caused deaths, 34% were from stroke and 26% from ischemic heart disease. For comparison, lung cancer accounted for only 6% of deaths.

“The risks from air pollution are now far greater than previously thought or understood, particularly for heart disease and strokes,” said Maria Neira, MD, Director of the Department for Public Health and Environment at the WHO, in a press release. William Zogbhi, MD, called the data “startling” and issued an appeal to “think globally but act regionally,” particularly as any reduction in air pollution will have multiple effects in terms of reducing CVD, cancers, and respiratory diseases.

“Laws that would decrease pollution—in whatever shape or form—will affect so many people at the same time. It’s almost like an effect en masse,” he said.

The new estimates are not only based on more knowledge about the diseases caused by air pollution, but also upon better assessment of human exposure to air pollutants through the use of improved measurements and technology. This has enabled scientists to make a more detailed analysis of health risks from a wider demographic spread that now includes rural as well as urban areas.

“Disease prevalence is much higher in South-Asia and the Western Pacific areas, where indoor pollution is primarily from cooking and heating in a home using coal, wood burning, and other sources that produce fumes,” said Dr. Zogbhi. “Outdoor pollution is your usual pollution because of energy production, waste management, and the like.”

Climate change also contributes to pollution-related CV risk. Heat amplifies the adverse impacts of ozone and particulates on CVD. These pollutants are likely to be affected by climate change mitigation activities, and thus, efforts to curb pollution will likely reduce rates of cardiovascular morbidity and mortality.

Prolonged drought, such as that currently complicating life in the Southwestern United States, will lead to more dust and particulate pollution while increased rainfall in other parts of the country will cleanse the air but may create more mold and microbial pollution. In addition, drought, declining water quality, and increased temperatures contribute to the growth of harmful algal blooms that produce toxins that can be aerosolized and exacerbate asthma and respiratory diseases.

The good news: The June 2, 2015, issue of JACC included a paper demonstrating that home air purification provides clear cardiopulmonary benefits among young, healthy adults in a Chinese city with severe ambient particulate air pollution. The benefits included significant decreases in both systolic and diastolic blood pressure.

Another break in the clouds: the recent NEIHS report on climate change notes that cardiovascular and stroke risks resulting from climate change could be offset by reductions in air pollution due to climate change mitigation.

It’s easy to shuck responsibility for reducing pollution in the Western world by simply saying, “Well, no matter what we do, there’s always China and India spewing tons of emissions.” And this is true, to some extent. China burns nearly half of the coal consumed on the planet and emits more greenhouse gases than anyone else. Industrial waste and human sewage clog the country’s waterways.

But Dr. Smith cautioned that this is a “let them eat cake” approach and suggested that a look back at the history of industrialization in the Western world tells a similar story of rapid industrialization leading to record amounts of pollution, including in the United States and England.

“There is a tension between having the economy to feed the people and develop the [desired] quality of life and yet not polluting the atmosphere,” he noted.

The Wounds of War

The effects of war in the 21st century are getting harder to ignore. Reaching far beyond the loss of life on the battlefield, which these days often encompass highly populated urban areas, stands the massive disruption to society: extreme poverty, millions of people displaced, unhygienic conditions, and scarcity of everything—food, water, medical care, electricity. Plus the psychological effects.

“The data show simplistically that if you’re living in a refugee camp, and I’ll take the example of the conflict in Syria now with about 2 million people migrating into Lebanon and quite a few to Jordan and Turkey, living in tents and with all the weather changes, that there are effects on total health but also cardiovascular health—lack of medications, lack of continuity, all these things,” said Dr. Zogbhi.

“No matter where you are in the world, war is similar. There is the acute effect and the lingering effect,” he said. “The priorities we take for granted—taking care of your health, taking medications, taking care of CV risk—these are all but eliminated and survival is the mode.”

Even in non-forced but large migrations, like the 700,000 to 800,000 individuals migrating to Texas each year looking for better economic opportunity, one sees issues with providing health care, added Dr. Smith. “Again, if you don’t have access to medications, prevention, including secondary prevention, then it will affect cardiovascular health,” he added.

Case Study: Syria

While it may be hard to imagine now, a few years ago, over 700,000 to 800,000 individuals migrating to Texas each year looking for better economic opportunity, one sees issues with providing health care, added Dr. Smith. “Again, if you don’t have access to medications, prevention, including secondary prevention, then it will affect cardiovascular health,” he added.

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- William Zogbhi, MD

successes in reducing events.

Recently, Newman and colleagues reported for the first time that fine particulate air pollution is also independently associated with carotid artery stenosis, an important risk factor for cerebrovascualr disease and stroke.9

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- William Zogbhi, MD
ago Syria served as a model for developing countries, which typically lack reliable health and risk factor surveillance. There was an analysis of cardiovascular health among adults in Syria published in 2007,\(^6\) which in and of itself showed that while there once was functioning health care in the country, Syrians also exhibited a very high prevalence of risk factors for CVD. This study projected that about 85% of deaths in Syria would be related to CVD in the decade ending in 2016.

M. Zaher Sahloul, MD, a pulmonologist from the University of Chicago, Illinois, was born in Syria and immigrated to the United States 25 years ago. He is also the president of the Syrian American Medical Society (SAMS), which treated 1.3 million patients in Syria in 2014. He shared at ACC.15 some frankly shocking data on the state of health care in Syria today.

It is, quite literally, a dark time for Syria. After 4 years of civil war, 83% of the population is without electricity, 4 out of 5 Syrians live below poverty, and life expectancy has decreased from 75.9 year to 55.6 years (or 27% of life lost). A full 6% of the population have been killed, maimed, or injured.

Beyond injury and trauma—and in the case of Syria, the United Nations (UN) recently confirmed 72 uses of chlorine gas on civilian populations—war brings increased morbidity and mortality from non-communicable diseases, and resurgence of infectious disease due to decreased levels of vaccination, epidemics of infectious disease, and parasitic disease related to disintegration of public health systems and lack of clean water and electricity.

“So, for example, in Aleppo, which is the largest city in Syria, there is no garbage collection or disposal, and because of that we have seen an increase in leishmaniasis, lice, and scabies,” said Dr. Sahloul.

A return to the Dark Ages may be the best way to describe this situation, because it will take years, perhaps generations, to recover. Somewhat unique to these kinds of crises, noted Dr. Sahloul, Syria has experienced a systematic destruction of health care and the public health infrastructure, including the targeting of doctors, ambulances, and hospitals. These attacks have led to a dramatic reduction in medical personnel. “Before the crisis, we had about 30,000 physicians in Syria,” said Dr. Sahloul. “According to the WHO, we have about 15,000 physicians in Syria now, and that number is dropping by the day.

“The public health system is overwhelmed by the crisis, by the trauma, and the violence...” said Dr. Sahloul.

As of March 12, 2015, Physicians for Human Rights documented that 610 Syrian medical personnel had been killed in the last 4 years, with 139 of them tortured to death or executed, as well as 233 attacks on medical facilities, 88% of them by governmental forces. Of the 1,171 doctors practicing in Ministry of Health hospitals in the Aleppo Governorate, only 292 remained as of September 2014.

Just as climate change contributes to pollution (and pollution-related CVD risk), global warming contributed greatly to the situation in Syria. Dr. Sahloul noted that in the 8-year span between 2005 and 2010, Syria experienced its worst drought in the last 10,000 years; this led to the displacement of about 2 million people. According to several studies, the net urban influx resulting from the drought is considered to be a causal factor in the 2011 uprising that led to the prolonged and continuing civil war.

**Humanitarian Crises**

Syria is far from the only country dealing internal strife on a massive level. The UN and its humanitarian partners are currently responding to four Level 3 emergencies (not counting Ebola): Syria, Iraq, Central African Republic (CAR), and South Sudan. Level 3 is the UN classification for the most severe, wide-ranging humanitarian crises based on scale, urgency, and complexity of the needs, coupled with the lack of domestic capacity to respond.

The numbers are staggering: 7.6 million displaced in Syria, 2.5 million in Iraq due to fighting between ISIS and government troops; 2.7 in CAR, and 1.5 million in South Sudan.\(^7\)

According to more UN data, by the beginning of 2014, there were 51.2 million people forcibly displaced, which is the highest on record since the refugee crisis that followed World War II. Syria alone accounted for about 9 million of these refugees.\(^8\) For perspective, the population of Spain is just over 47.2 million; South Korea has a population of 50.2 million.
A Call to Action
At the end of his talk at ACC.15, Dr. Sahloul queried the audience on their willingness to participate in medical missions to help patients and refugees in areas of conflict. A full 80% of the audience (albeit a select group, given the fact they chose to attend the session) expressed willingness. Dr. Sahloul stressed that there are safer places to help serve than Syria and volunteers would be sent to less treacherous locations.

In his presidential address at the opening of ACC.15, Immediate Past-President Patrick O’Gara, MD, called upon the ACC and other societies “to lead during a time that seems to be completely devoid of compromise, and in a place where often community interests seem to be subordinated to individual rights.”

“It’s easy to think at times that we operate in a vacuum, especially when we come to national meetings. But we live in a world of chaos; we live in a world of terrorism, climate change, air pollution, dwindling resources, intolerance, and inequality,” said Dr. O’Gara, showing this slide (FIGURE 1).

“Once you think [about it,] there is a bigger picture confronting us and therefore a greater responsibility.”

References:

What Does a Level 3 Emergency Look Like?
Syria
- Destruction of health care and public health infrastructure
- Indiscriminate aerial bombing of civilian areas by barrel bombs, cluster bombs and ballistic missiles
- Chemical weapons systematic use
- Targeting of doctors, ambulances and hospitals
- Flight of health care professionals
- First polio epidemic since 1999
- More than 300,000 deaths due to NCDs

Systematic Attacks on Syrian Health Care
According to Physicians for Human Rights, as of March 12, 2015:
- 233 deliberate or indiscriminate attacks on 183 medical facilities
- 610 Syrian medical personnel have been killed
- 139 of workers were tortured to death or executed
- 97% of workers were killed by government forces
- On average a medical worker was killed every other day in Syria in 2014
- Of the 1,711 doctors practicing in Ministry of Health hospitals in Aleppo Governorate, only 292 remained as of September 2014

Systematic attacks on health care infrastructure occur frequently in Syria, including attacks on doctors, hospitals, and ambulances.
Lessons Learned: Reflections of a Cardiovascular Nurse

Each profession needs to direct its own practice, govern itself, and mentor junior professionals.

I read with interest the recent 2015 ACC Health Policy Statement on Cardiovascular Team-Based Care and the Role of Advanced Practice Providers, notably chaired by a physician and an advanced practice nurse, and co-authored by a team that represents the disciplines of medicine, nursing, pharmacy and physicians assistants. I extend my congratulations to the writing team and to the college for its work over the past 12 years in welcoming registered nurses (RNs), advanced practice nurses (APNs), pharmacists, and physician assistants (PAs) as members of the ACC! As an APN who was among the first to become an ACC member in 2003 and participate actively in committee work, this document is a welcome addition to the library of health policy statements. Reflecting on the past 12 years, there has clearly been an evolution in the depth of the incorporation of non-physician professionals as ACC members. Those of us who have been part of this journey have also learned some important lessons.

Culture

Each profession has its own distinct culture. Retaining that culture allows the team to leverage the respective strengths of each to develop a superior clinical team. All of us involved in organizational changes like this need a measure of cultural competence to navigate these new interdisciplinary relationships. Since the ACC first welcomed RNs, APNs, PAs, and pharmacists as ACC members, all of the stakeholders have grown in awareness of the culture of the other disciplines. Initially, the College, in an effort to choose an appropriate term to describe the new non-physician members, created the membership category “cardiac care associates.” The term has since been replaced by cardiovascular team (CVT) section. Nurses, PAs, and pharmacists have a large measure of professional pride in their respective professional groups, and greatly value their association to their profession, their education, professional designation, and licensure. Most were not fans of the term “cardiac care associate,” a well-intentioned but unfortunate term created to describe the new non-physician membership category (in much the same way that most of APNs cringe at the term “mid-level” or “physician extender”). None of these terms was coined to be pejorative, but like any group with a strong culture and identity, terms do matter to us, and names are not inconsequential.

When the ACC initially welcomed nurses as members, it was required that applicants for membership be recommended by a physician colleague. While this was consistent with requirement for physicians seeking ACC membership also, the requirement alienated some would-be ACC nurse members. Nurses were not accustomed to requiring a sponsor to become a member of a professional organization. A recommendation by a current ACC member is still required for nurses applying for membership, but a recommendation letter can now come from another CVT member. I believe this inclusive change has served to help grow the nursing membership.

Concurrently, I believe that CVT members have grown in respect for the tradition and history of the ACC. A membership of 4,600 CVS members is impressive; however, this is part of an overall ACC membership numbering nearly 50,000! The ACC is a 65-year-old organization with a deep and proud history whose identity has changed by the altered complexion of its membership over these past 12 years. Membership-wide acceptance of the inclusiveness we have enjoyed does not happen overnight. But now, in 2015, nurses, APNs, PAs and pharmacists are an active part of many/most committees, councils and writing groups. Those of us who have been active participants and leaders in the college have cultivated alliances and invested in relationships with physician colleagues that have helped us to participate and also to lead effectively and credibly. This mutual respect between and among professions is a key component of cultural competence.

Professional Direction and Mentorship from Our Own

Each profession needs to direct its own practice, govern itself, and mentor junior professionals. APNs, RNs, and PAs appropriately look to their physician colleagues for their clinical expertise in a collaborative practice setting. It is important, however, that we remember to seek the counsel of mentors and senior leaders in our own respective professions for career advice, leadership, scope of practice issues and overall direction. Those of us in more senior career stages need to take “to heart” our responsibility as mentors to emerging leaders by modeling a collaborative and collegial interface with all team members. Importantly, in order that our profession remains competitive in recruiting and retaining promising future cardiovascular nursing leaders, we need to be attentive to the four key messages of the Institute of Medicine’s Future of Nursing:

1. Nurses should practice to the full extent of their education and training.
2. Nurses should achieve higher levels of education and training through an improved education system that promotes seamless academic progression.

3. Nurses should be full partners, with physicians and other health professionals, in redesigning health care in the United States.

4. Effective workforce planning and policy making require better data collection and an improved information infrastructure.

Likewise, APNs, RNs, PAs, and pharmacists need to look to their professional organizations for advocacy issues important to their own unique professions. Active cardiovascular clinical professionals should join, or, at minimum, engage with, their own professional societies to engage in advocacy issues that impact the nursing profession. The American Nurses Association (ANA) and the American Association of Nurse Practitioners (AANP) represent the interests of nurses and nurse practitioners respectively. Additionally, cardiovascular subspecialty nursing organizations like the American Association of Heart Failure Nurses (AAHFN), the Society for Vascular Nursing (SVN), and the Preventive Cardiovascular Nurses Association (PCNA) add value with in-place and virtual and on-demand continuing education opportunities and patient education tools. Each of these organizations brings important value that nurses in subspecialty cardiovascular practice settings can leverage to enhance their clinical practices.

Additionally, involvement in the American Heart Association (AHA) can add an additional dimension in terms of both national and local volunteerism and advocacy in the public health domain.

The ACC took an important leadership position when, in 2008, the college worked with the ANA to convene a group of nursing leaders to publish Cardiovascular Nursing: Scope and Standards of Practice.4 This was a very important step in the development of collegial relationship with cardiovascular nursing organizations, one that helped to form a strong basis for ongoing liaison relationships that have helped to strengthen professional education efforts. We are all in competition for the same members, but we have been able to identify numerous opportunities for collaboration-opportunities that have strengthened and added value to our individual efforts—and have certainly impacted the quality of cardiovascular care.

It Takes a Village

The demands of our current system are increasing every year. We need increased resources for interactions with third party payers, registries, data warehouses, and others to assure coordination of care between and among providers and systems. We have important roles in coaching patient to improve self-care management and adherence. To accomplish all that is required of us during the always too-short acute care stay or ambulatory clinical encounter, we need to leverage all members of the team. The ACC has gathered the key stakeholders, but there are others we need to incorporate into the team to satisfy the six aims of high quality care-care that should be safe, effective, patient-centered, timely, efficient and equitable.5

In patient-centered medical home (PCMH)6 practice redesign tactics, the team includes not only physicians, pharmacists, PAs, APRNs, and RNs, but it includes support staff as well. For example, front desk scheduling staff can encourage patients to arrive for their visits armed with pertinent documents like home blood pressure records and questions for the clinician and can direct them in accessing important community resources as needed. The medical assistant who “rooms” the patient can support self-care management by reinforcing health messages and encouraging the patient and his/her care partner to have questions and concerns ready to discuss with the clinician. All of these team members can increase the likelihood that clinical professionals will utilize their time with the patient in a practice that takes full advantage of their knowledge and training-working to the limit of their licensure.

Strategies that increase patient-centeredness, engagement, and involvement in self-care are all great concepts, but they demand learning new ways of thinking and doing.

In our metrics-focused environment, we also need to increasingly leverage the talents of our non-clinical professional colleagues from the engineering world who design, analyze, and measure a complex system in order to improve its safety, timeliness, efficiency and effectiveness.7 These are the professionals who, with our clinical input, create systems that make “the right thing to do the easy thing to do.”

In the End, It’s Not All About Us

All cardiovascular clinicians are struggling with professional practice issues today. We are overwhelmed with the amount of time and work that documentation requires, and the work of scrupulous medication reconciliation. Physicians struggle with maintenance of certification and declining reimbursement. APRNs struggle with state to state variation in scope of practice issues. Many RNs are returning for school for additional education at the masters’ level to attain a higher level of job security. Strategies that increase patient centeredness, engagement, and involvement in self-care are all great concepts, but they demand learning new ways of thinking and doing; they require more of the scarcest commodity we have today: our time. But for all of the issues facing our professional groups individually and collectively, in the end, it's not about championing or advocating for our individual professional groups. It's really all about improving outcomes for the most important member of the health care team: the patient.

REFERENCES


Suzanne Hughes, MSN, RN, is Chief Learning Officer at the Preventive Cardiovascular Nurses Association.
A pulmonary embolism may lead to an unfamiliar, serious consequence.\(^1,2\)

As many as 1 out of every 25 of your previously treated PE patients (>3 months of anticoagulation\(^3\)) may develop chronic thromboembolic pulmonary hypertension, or CTEPH.\(^1,4^*\)

A ventilation-perfusion (V/Q) scan can rule out CTEPH in PE patients with chronic symptoms\(^5\) after >3 months of anticoagulation.\(^3\)

**If you know what to look for, a V/Q scan makes it relatively easy to spot.**\(^5\)

*Based on a study with 223 patients in which 3.8% were diagnosed with CTEPH within 2 years of their first episode of pulmonary embolism with or without prior deep-vein thrombosis (95% CI, 1.1 to 6.5). CTEPH did not develop after two years in any of the 132 remaining patients with more than 2 years of follow up.

References:
Suspecting and Screening for PH After PE ... It May Be CTEPH

Acute pulmonary embolism can become chronically complicated

presented by

Raymond L. Benza, MD

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I t has been estimated that there may be as many as 600,000 episodes of acute PE in the US each year. For as many as a quarter of patients who experience an acute PE, the initial clinical presentation is sudden death owing to right ventricular failure.\textsuperscript{7} For those patients who survive an acute PE, the symptoms include shortness of breath, pleuritic pain, and cough. Patients with a first episode of acute PE who have stable hemodynamics can have good survival rates when they are anticoagulated for at least 3 months.\textsuperscript{8}

But even with adequate anticoagulation, some survivors of acute PE have lasting complications and associated symptoms.\textsuperscript{9} Recently, Klok et al have coined the term “post-pulmonary embolism syndrome” to describe chronic complications of PE, involving permanent changes in pulmonary hemodynamics (artery flow, pulmonary gas exchange and/or cardiac function) which are associated with shortness of breath and decreased exercise capacity.\textsuperscript{9} The most serious manifestation of this syndrome—and the most serious complication of acute PE—is chronic thromboembolic pulmonary hypertension, or CTEPH.\textsuperscript{2,6}

HOW COMMON IS CTEPH?

Based on data from small observational studies that followed survivors of acute PE, incidence of CTEPH has been estimated to be 0.57% (N=866 survivors of acute PE observed) to 3.8% (N=314 survivors of acute PE observed).\textsuperscript{10} A more recent, but smaller (N=146 acute PE survivors followed for 26 months), study found that 8 survivors of acute PE were suspected to have CTEPH, and 7 of these patients were confirmed to have CTEPH.\textsuperscript{11} Yet another study of survivors of acute PE (N=104) saw 5.8% of patients develop CTEPH within 2 years. Further follow-up saw an additional 4 cases develop beyond 2 years (time period not specified) for a total of 9.1% of the original study population.\textsuperscript{12}

The absence of prior acute PE does not exclude a diagnosis of CTEPH\textsuperscript{10,12}

Applying even the lower end of this range of estimates to the annual population of survivors of acute PE suggests there could be thousands of incident cases of CTEPH each year in the US. Further, though CTEPH is a complication of a single or recurrent PE, as many as 25% to 30% of patients who have CTEPH may never have had an overt PE or a history suggestive of PE.\textsuperscript{10,11} The true incidence of CTEPH may, therefore, be underestimated, because postembolism observational studies do not include patients without a history of PE.\textsuperscript{11}

CTEPH IS A FORM OF PULMONARY HYPERTENSION

Chronic thromboembolic pulmonary hypertension is a form of pulmonary hypertension (PH), designated by the World Health Organization as Group 4 PH. There are 5 WHO Groups of PH: \textsuperscript{13}

1: Pulmonary arterial hypertension
2: PH due to left heart disease
3: PH due to lung diseases and/or hypoxia
4: CTEPH
5: PH with unclear multifactorial mechanisms

CTEPH results after a single or recurrent pulmonary embolism (PE) that creates chronic blood clots which obstruct or substantially narrow pulmonary arteries.\textsuperscript{14} This obstruction and narrowing increases both pulmonary arterial pressure (PAP) and pulmonary vascular resistance (PVR) to abnormal levels.\textsuperscript{15} Hemodynamically, CTEPH is most often defined as a mean PAP ≥25 mmHg, with pulmonary capillary wedge pressure ≤15 mmHg. Over time, narrowing of small pulmonary vessels can lead to right ventricular afterload, progression of PH, and CTEPH.\textsuperscript{16} If CTEPH is unrecognized or left untreated, right ventricular dysfunction can progress, ultimately resulting in right heart failure.\textsuperscript{17}

WHEN TO SUSPECT CTEPH

Symptoms of CTEPH are nonspecific\textsuperscript{18} and include dyspnea on exertion, fatigue, weakness, chest pain, syncope, hemoptysis, and lower-extremity edema.\textsuperscript{19} Among the risk factors for CTEPH are unprovoked or recurrent PE, young age at the time of first PE, and splenectomy.\textsuperscript{18} As many as 1 in 25 survivors of acute PE may go on to develop CTEPH within 2 years,\textsuperscript{16} so it is essential to screen for CTEPH in patients who have still have symptoms of dyspnea or decreased exercise capacity 3 or more months after acute PE despite effective anticoagulation.\textsuperscript{17}

HOW DO WE DIAGNOSE CTEPH?

Computed tomographic pulmonary angiography (CTPA) has become the standard diagnostic test for acute PE, and a good-quality CTPA that is negative for acute PE effectively rules that diagnosis out.\textsuperscript{20} Unlike for acute PE, though, CTPA is not preferred as a diagnostic test for CTEPH.\textsuperscript{17} Instead, the ventilation/perfusion, or V/Q, scan is the preferred and recommended screening test for CTEPH.\textsuperscript{17} The V/Q scan has been shown to have >96% sensitivity, meaning that a negative (ie, normal) V/Q scan essentially rules out the presence of CTEPH.\textsuperscript{17} Conversely, in the same study, CTPA had a sensitivity of only 51% as a screening test for CTEPH.\textsuperscript{17} Multiple national and international guidelines recommend the use of the V/Q scan as the CTEPH screening tool of choice.\textsuperscript{4,15,20-22} If there is reason to suspect CTEPH in a survivor of acute PE and V/Q scanning is not readily available, the patient should be referred to a center that can perform a V/Q scan.

An abnormal V/Q scan suggestive of blood clots is not enough on its own to diagnose CTEPH. To confirm CTEPH, right heart catheterization (RHC) must be performed to confirm mean PAP ≥25 mmHg, with a pulmonary capillary wedge pressure (PCWP) ≤15 mmHg. Selective pulmonary angiography is typically used to confirm presence and location of CTEPH lesions.\textsuperscript{11,22} CTPA and magnetic resonance angiography can contribute complementary information on the lesions, their surroundings, and their accessibility.\textsuperscript{22}

TREATING CTEPH IN SURGICAL CANDIDATES

Referral of CTEPH patients to PH centers for confirmation of diagnosis, operability assessment, and comprehensive care is essential.\textsuperscript{23} PTE surgery is the first-line treatment of choice for surgical candidates with CTEPH, because it is potentially curative.\textsuperscript{10,12,23} Once the diagnosis of CTEPH is confirmed, all CTEPH patients must be assessed for operability by an experienced CTEPH team that would plan, perform, and follow-up the patient’s surgery. Operability assessment must consider the patient’s risk, including quality of and accessibility of lesions, hemodynamic assessment, and consideration of comorbidities and patient characteristics.\textsuperscript{11} If one experienced CTEPH team determines that a patient has inoperable disease, a corroborating opinion from a second experienced CTEPH team should be secured, if possible.\textsuperscript{15} This is because operability assessment is subj ective, and what may be deemed by one experienced CTEPH team as inoperable disease may well be deemed operable by another experienced CTEPH team.

PTE surgery is the first-line treatment of choice for surgical candidates who have CTEPH\textsuperscript{16}
Patients who have operable CTEPH should be referred for surgery without delay. Though all CTEPH patients require lifelong anticoagulation to prevent in situ pulmonary artery thrombosis and recurrent venous thromboembolism, anticoagulation is not sufficient to treat the progressive right ventricular dysfunction that results from CTEPH. Similarly, there is no evidence that there is benefit derived from using “bridging” therapy with PAH-specific drugs in patients with operable CTEPH. PTE surgery allows for the removal of central blood clots, resulting in improvement and often normalization of pulmonary function. About two-thirds of patients have normal hemodynamics following PTE.

**REFERENCES**


*Based on a study with 223 patients in which 3.8% were diagnosed with CTEPH within 2 years of their first episode of pulmonary embolism with or without prior deep-vein thrombosis (95% CI, 1.1 to 6.5).*
Anthony Atala, MD, is the Director of the Wake Forest Institute for Regenerative Medicine and the W.H. Boyce Professor and Chair of the Department of Urology at Wake Forest Baptist Medical Center. A practicing surgeon and a researcher in the area of regenerative medicine, his current work focuses on growing new human cells, tissues, and organs. Dr. Atala went to medical school at the University of Louisville, where he also completed his residency in urology, and lead the team that developed the first lab-grown organ—a bladder—to be implanted into a human. Under his leadership, his team has also successfully implanted engineered cartilage, urethras, and vaginas into patients. Dr. Atala's work was listed as Time magazine's top 10 medical breakthroughs of the year, and he was featured in U.S. News & World Report as one of 14 Pioneers of Medical Progress in the 21st Century. He is the editor of 12 books, has published more than 400 journal articles, and has applied for or received over 200 national and international patents. He recently published a Viewpoint article in JAMA entitled “Regenerative Medicine.”

How did you first become interested in the field of regenerative medicine? I'm a pediatric urological surgeon by training, and my interest in regenerative medicine was first piqued in 1990 when the standard of care for adult patients with bladder cancer was to fashion a reservoir made out of intestine to replace the bladder. While the intestine was designed to absorb nutrients from food and excrete the waste, the bladder however only excretes and does not absorb. This surgery resulted in the patients absorbing things that they should have been excreting, leading to chemical imbalances, stones, perforations, and increased tumors. As pediatric urologic surgical specialists, we were applying this same procedure to children with spina bifida who had an 80-year life expectancy, leaving the child with a long life of potential medical challenges because intestinal tissue simply didn’t belong there. The thought was that the ideal solution would be to put in an organ that had the same qualities as the bladder, and we began to wonder about the possibility of engineering an organ using the patient’s own cells.

What breakthrough advancements have you seen in the past couple of decades? Some of the important advancements in our field include the development of iPS cells, increased knowledge in materials science, clinical studies of regenerative medicine therapies, and the advancement of 3D bioprinting. I will elaborate on a few of these. Advances in biomaterials science are important because biomaterials must match the structural, architectural, and biological properties of the tissues we are trying to replace. Creating bone requires a very different biomaterial than creating blood vessels. For the blood vessel, the biomaterial must be elastic and resilient, but bone must also be strong enough to withstand large amounts of pressure. An increased understanding of biomaterials helps ensure success of the engineered organ. In the area of clinical trials and pilot studies, successful studies of new regenerative medicine applications have opened the door to further expanding the number of diseases that can be treated in this way. 3D bioprinting is important because it is a way of scaling up the process of engineering replacement tissues in the lab. Because of its precision and reproducibility, it offers the potential for the successful dissemination and widespread use of regenerative medicine therapies that so far have been offered to patients only through small clinical trials.

In your 2009 Ted Talk you show footage of a printer that is able to generate a two-chamber heart in about 40 minutes. How much closer
have we come in the past 6 years to being able to clinically apply this technology?
The video you mention showed a proof-of-concept study in which we used a modified ink jet printer to print a multi-chambered structure. Today, we’re using 3D printers that we design in-house to print tissues that are being tested pre-clinically and to print a system of mini organoids that will be used to test drugs.

What are some of the challenges to growing new organs?
Regenerative medicine researchers have successfully implanted three types of organs and tissues. The simplest tissues to build are the flat structures such as skin. Tubular structures such as blood vessels and urethras are more complex because they need two major cell types. Hollow organs like the bladder, uterus, or stomach have two major cell types, but have a more complex architecture and functionality, so they fall into a third level of complexity. The solid organs usually have more than two cell types and require a lot more vascularity because there are so many more cells per centimeter than in any of the other tissue types. Vascularizing solid tissues is a challenge that we are working to resolve.

At the end of the day, we have to remember that our goal is to make patients better. In some cases, we may be able to accomplish that goal without growing an entire new organ. We are also exploring the possibility of tissue patches, or inserts, to restore organ function, as well as cell therapies. Time will tell which strategy is best.

Please tell us a bit about the “Body on a Chip” project at the Institute for Regenerative Medicine.
This project, funded by the Defense Threat Reduction Agency, has the goal of building a miniaturized system of human organs to model the body’s response to harmful agents and to develop potential therapies. This approach has the potential to reduce the need for testing in animals, which is expensive, slow, and has results that aren’t always applicable to people. This project involves five institutions across the country and will develop mini hearts, livers, lungs, and blood vessels that will be linked together with a circulating blood substitute. The organ structures will be placed on a chip so that sensors can provide online monitoring of individual organs and the overall organ system.

As you mention in your recent *JAMA Viewpoint* article, the U.S. Department of Health and Human Services calls regenerative medicine the “next evolution of medical treatments” and predicts that regenerative medicine will be the “vanguard of the 21st century health care.” What innovations do you predict in the next couple of decades? How will the field of cardiology be affected?
I do foresee a day when we’ll be able to replace certain tissues and organs with engineered tissue and when cell therapies will be routinely used to restore function. We know that these technologies can work through clinical trials on various tissues. What we are focusing on now is expanding the number of conditions that can be treated and bringing the treatments to larger groups of patients. It is difficult to predict exactly how cardiology will be affected, but the cardiovascular system is obviously an area of focus for regenerative medicine scientists around the world.

Katlyn Nemani, MD, is a physician at New York University.
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**How did you come up with the idea for FeetMe?**

Broadly speaking, I have long been interested in creating new, cost-effective medical devices that improve patient care, and recognized that doing so requires a collaborative approach that focuses on the needs of patients, physicians, and the health care industry as a whole. I saw an opportunity to do so with FeetMe.

While I was a student at Ecole Polytechnique, I spent some time with diabetic patients at a nearby hospital, La Pitié Salpêtrière, Paris, France. Professor Agnes Hartemann and Dr. Georges Ha-Van opened my eyes to how painful and devastating foot ulcers and peripheral wounds can be to these patients. I could not understand how, with all of the technology available today, we could not prevent these situations.

As an engineer, I tried to envision how technology could help these patients. If we could restore their peripheral sensitivity we’d be able to help them avoid putting too much prolonged pressure on their feet, which leads to the ulcers. To this end, my colleagues and I decided to design a connected pressure-sensor that would supplement the damaged nerves of the neuropathy. Combined with a machine-learning algorithm that analyzes the pressure data that we collect, this sensor would enable us to alert the patient if there was increased risk of an ulcer.

**What medical problems are you trying to solve?**

Plantar pressure measurements are used today in a variety of clinical situations by podiatrists: for example, for post-surgery biomechanical assessment, intra-operative assessment, orthotics design, and assessment of plantar pressure to prevent this problem.

We realized that ambulatory measurements of the plantar pressure would bring even more value in the prevention of ulcers among patients suffering from neuropathy. Diabetes is quickly growing in prevalence, with 8% more cases developing year-to-year. Among several complications, loss of sensitivity in the extremities—or diabetic neuropathy—can be one of the most damaging. Ulcers that result from neuropathy may even lead to gangrenous infection and amputation. In fact, more than 1,000,000 diabetics are amputated each year, with 100,000 in the U.S. alone. There is currently no effective and cheap tool that measures the plantar pressure to prevent this problem.

Our solution aims to make plantar pressure assessment an affordable tool for both clinicians and patients.

**How can cardiologists and their patients benefit from FeetMe?**

One case is in monitoring patients with peripheral edema, as a result of, for example, congestive heart failure (CHF). These patients may also develop ulcers if they have any abnormal pressure issues. We believe FeetMe can also be used to effectively monitor these patients who are at risk for ulcers.

Since cardiovascular disease is the leading cause of morbidity and mortality in people with diabetes mellitus, we know that cardiologists often treat diabetic patients. Patients with diabetes mellitus have a two- to four-fold increase in the risk of developing cardiovascular disease than those without diabetes mellitus, and also a two- to five-fold increase in mortality attributable to cardiovascular disease when compared with age- and sex-matched non-diabetic patients. Accelerated atherogenesis, blood abnormalities (altered platelet function, inflammation, hypofibrinolysis, and hypercoagulability), and myocardial vulnerability in diabetic patients are now considered causative factors for life-threatening cardiovascular events.

It’s important for cardiologists to help their patients maintain good overall health. For their diabetic patients at risk for pressure ulcers, this includes feet health. That being said, our first targeted users are diabetic patients and podiatrists.

**Can you describe how your technology works?**

We have developed a disruptive capacitive pressure sensor technology that allows for a high resolution mapping of the foot. We collect data at a high frequency and transmit it via Bluetooth to a smartphone or a brother device. We apply our machine-learning algorithm to this data to evaluate walking patterns and send an alert to the patient if needed.

**What is your stage of prototyping/piloting the product in a clinical setting?**

We are in the middle of the CE mark process that will come in June and we have started a first clinical trial at La Pitié Salpêtrière Hospital in Paris, France.

**What is your background in medicine & technology?**

I’m a former student at Ecole Polytechnique and UC Berkeley in Engineering (MS). My co-founder, Maxime Fournier, COO, has an MS in Biomedical Engineering from UCLA and our other co-founder, Andrey Mostovoy, CTO, PhD, trained at Ecole Polytechnique and INSEAD. We have created very strong relationships with Hospital de la Pitié Salpêtrière where we spent a lot of time designing the product.

**Shiv Gaglani** is an MD/MBA candidate at the Johns Hopkins School of Medicine and Harvard Business School. He writes about trends in medicine and technology and has had his work published in Medgadget, The Atlantic, and Emergency Physicians Monthly.
Adverse Reactions:
The most common adverse reactions reported at least 1% more frequently with Corlanor® than placebo and that occurred in more than 1% of patients treated with Corlanor® were bradycardia (10% vs. 2.2%), hypertension or increased blood pressure (8.9% vs. 7.8%), atrial fibrillation (8.3% vs. 6.6%), and luminous phenomena (phosphenes) or visual brightness (2.8% vs. 0.5%).

Please see Brief Summary of full Prescribing Information on following page.

References:

BPM = beats per minute; CV = cardiovascular; HF = heart failure; LVEF = left ventricular ejection fraction.

Bradycardia and Conduction Disturbances:
Bradycardia, sinus arrest and heart block have occurred with Corlanor®. The rate of bradycardia in patients treated with Corlanor® compared to placebo was 6% (2.7% symptomatic; 3.4% asymptomatic) vs. 1.3% per patient-year, respectively. Risk factors for bradycardia include sinus node dysfunction, conduction defects, ventricular dyssynchrony, and use of other negative chronotropes. Concurrent use of verapamil or diltiazem also increases Corlanor® exposure, contributes to heart rate lowering, and should be avoided. Avoid use of Corlanor® in patients with 2nd degree atrioventricular block unless a functioning demand pacemaker is present.

For patients with stable, symptomatic chronic HF with LVEF ≤ 35% and in sinus rhythm with resting heart rate ≥ 70 bpm:

Corlanor® significantly reduced the relative risk of hospitalization for worsening HF or CV death by 18%, 4.2% ARR, (P < 0.0001).1,2

– Composite endpoint result reflected only a reduction in the risk of hospitalization for worsening HF with no favorable effect on CV death

Indication
Corlanor® (IVabradine) is indicated to reduce the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction ≤ 35%, who are in sinus rhythm with resting heart rate ≥ 70 beats per minute and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use.

Important Safety Information
• Contraindications: Corlanor® is contraindicated in patients with acute decompensated heart failure, blood pressure < 90/50 mmHg, sick sinus syndrome, sinoatrial block, 3rd degree atrioventricular block (unless a functioning demand pacemaker is present), a resting heart rate < 60 bpm prior to treatment, severe hepatic impairment, pacemaker dependence (heart rate maintained exclusively by the pacemaker), and concomitant use of strong cytochrome P450 3A4 (CYP3A4) inhibitors.
• Fetal Toxicity: Corlanor® may cause fetal toxicity when administered to a pregnant woman based on embryo-fetal toxicity and cardiac teratogenic effects observed in animal studies. Advise females to use effective contraception when taking Corlanor®.
• Atrial Fibrillation: Corlanor® increases the risk of atrial fibrillation. The rate of atrial fibrillation in patients treated with Corlanor® compared to placebo was 5% vs. 3.9% per patient-year, respectively. Regularly monitor cardiac rhythm. Discontinue Corlanor® if atrial fibrillation develops.
Adverse Reactions: The most common adverse reactions reported at least 1% more frequently with Corlanor® than placebo and that occurred in more than 1% of patients treated with Corlanor® were bradycardia (10% vs. 2.2%), hypertension or increased blood pressure (8.9% vs. 7.8%), atrial fibrillation (8.3% vs. 6.6%), and luminous phenomena (phosphenes) or visual brightness (2.8% vs. 0.5%).


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Adverse Reactions: The most common adverse reactions reported at least 1% more frequently with Corlanor® than placebo and that occurred in more than 1% of patients treated with Corlanor® were bradycardia (10% vs. 2.2%), hypertension or increased blood pressure (8.9% vs. 7.8%), atrial fibrillation (8.3% vs. 6.6%), and luminous phenomena (phosphenes) or visual brightness (2.8% vs. 0.5%).

Please see Brief Summary of full Prescribing Information on following page.


BPM = beats per minute; CV = cardiovascular; HF = heart failure; LVEF = left ventricular ejection fraction.
Corlanor® (ivabradine)

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Please see package insert for full Prescribing Information

1. INDICATIONS AND USAGE

Corlanor is indicated to reduce the risk of hospitalization for worsening heart failure in patients with stable, symptomatic chronic heart failure with left ventricular ejection fraction < 30%, who are in sinus rhythm with resting heart rate ≥ 70 beats per minute and either are on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use.

4. CONTRAINDICATIONS

Contraindication is contraindicated in patients with:

- Acute decompensated heart failure
- Blood pressure less than 90/50 mmHg
- Sick sinus syndrome, sinoatrial block, or 2° or 3° AV block, unless a functioning demand pacemaker is present
- Resting heart rate less than 60 bpm prior to treatment [see Warnings and Precautions (5.3)]
- Severe hepatic impairment [see Use in Specific Populations (8.7)]
- Pacemaker dependence (heart rate maintained exclusively by the pacemaker) [see Drug Interactions (7.1)]

5. WARNINGS AND PRECAUTIONS

5.1 Fetal Toxicity

Corlanor may cause fetal toxicity when administered to a pregnant woman. In animal studies in rabbits, and cardiac teratogenic effects were observed in fetuses of pregnant rats treated during organogenesis at exposures 1 to 3 times the human exposure [AUC(0-24)] at the maximum recommended dose [see Animal Data (6.2)]. Advice females to use effective contraception when taking Corlanor [see Use in Specific Populations (8.6)].

5.2 Atrial Fibrillation

Corlanor increases the risk of atrial fibrillation. In SHIFT, the rate of atrial fibrillation was 5.0% per patient-year in patients treated with Corlanor and 3.9% per patient-year in patients treated with placebo [see Clinical Studies (14)]. Regularly monitor cardiac rhythm. Stop Corlanor if atrial fibrillation develops.

5.3 Bradycardia and Conduction Disturbances

Bradycardia, sinus arrest, and heart block have occurred with Corlanor. The rate of bradycardia was 6.0% per patient-year in patients treated with Corlanor and 3.9% per patient-year in patients treated with placebo [see Clinical Studies (14)]. Regularly monitor cardiac rhythm. Avoid Corlanor if atrial fibrillation develops.

6. ADVERSE REACTIONS

6.1 Clinical Trials Experience

Common adverse reactions that appear in the following table:

- Cardiac Toxicity [see Warnings and Precautions (5.1)]
- Atrial Fibrillation [see Warnings and Precautions (5.2)]
- Bradycardia and Conduction Disturbances [see Warnings and Precautions (8.3)]

6.1.1 Clinical Trials Experience

In pregnant rabbits, oral administration of ivabradine during the first trimester, second trimester, or third trimester resulted in fetal toxicity and congenital anomalies. In pregnant rats treated at dosages providing 1 to greater than 10 times the human exposure at the MRHD based on AUC(0-24), teratogenic effects including interventricular septal defect and complex anomalies of major arteries were observed at doses ≥ 2.3 mg/kg/d (equivalent to the human exposure at the MRHD based on AUC(0-24)). In pregnant rabbits, oral administration of ivabradine during the period of organogenesis (gestation day 6-15) at doses of 2.3, 4.6, 9.3, or 19 mg/kg/d resulted in fetal toxicity and teratogenic effects. Increased intraperitoneal and post-natal mortality, and increased cardiac malformations were observed at doses ≥ 2.3 mg/kg/d (equivalent to the human exposure at the MRHD based on AUC(0-24)). In pregnant rats, oral administration of ivabradine during the period of organogenesis (gestation day 6-15) at doses of 2.3, 4.6, 9.3, or 19 mg/kg/d resulted in fetal toxicity and teratogenic effects. Increased intraperitoneal and post-natal mortality, and increased cardiac malformations were observed at doses ≥ 2.3 mg/kg/d (equivalent to the human exposure at the MRHD based on AUC(0-24)). In pregnant rabbits, oral administration of ivabradine during the period of organogenesis (gestation day 6-15) at doses of 2.3, 4.6, 9.3, or 19 mg/kg/d resulted in fetal toxicity and teratogenic effects. Increased intraperitoneal and post-natal mortality, and increased cardiac malformations were observed at doses ≥ 2.3 mg/kg/d (equivalent to the human exposure at the MRHD based on AUC(0-24)).

6.1.2 Postmarketing Experience

Luminous Phenomena (Phosphophens)

Phosphophens are phenomena described as a transiently enhanced brightness in a limited area of the visual field, halos, image distortion (strobo-pleurogenic, or pleuro-ophthalmic effects), or colored bright lights, or multiple images (retinal persistency). Phosphophens are usually triggered by sudden variations in light intensity. Corlanor can cause phosphophens, thought to be mediated through an abnormal retinal response to photoreceptors [see Clinical Pharmacology (12.1)]. Onset is generally within the first 2 months of treatment, after which they may occur repeatedly. Phosphophens were generally reported to be of mild to moderate intensity, and to treatment discontinuation in < 1% of patients, most resolved during or after treatment.

6.2 Postmarketing Experience

Because these reactions are volunteered from a population of uncertain size, it is not always possible to estimate their frequency reliably or establish a causal relationship to drug exposure. The following adverse reactions have been identified during post-approval use of Corlanor and are listed below by body system and frequency of reporting. While these events have been reported voluntarily from a population of uncertain size, there is no information regarding their frequency or relationship to drug exposure.

6.2.1 Body as a Whole

- Phosphenes, visual brightness

6.2.2 Cardiovascular System

- Hypertension, blood pressure increased

6.2.3 Digestive System

- Atrial fibrillation

6.2.4 Respiratory System

- Phosphenes, visual brightness

6.2.5 Skin and Appendages

- Phosphenes, visual brightness

6.2.6 Special Senses

- Phosphenes, visual brightness

6.2.7 Systemic Overdose

- Phosphenes, visual brightness

6.3 Overdose

Overdose may lead to severe and prolonged bradycardia. In the event of bradycardia with poor hemodynamic tolerance, temporary cardiac pacing may be required. Supportive treatment, including intravenous (IV) fluids, atropine, and intravenous beta-blockers, or agents such as isoproterenol, may be considered.

This Brief Summary is based on the Corlanor® Prescribing Information v1.04

Corlanor® (ivabradine)

Manufactured for: Amgen Inc.

One Amgen Center Drive

Thousand Oaks, California 91320-1799

Patent: http://pat.amgen.com/Corlanor/

AMGEN

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Phosphenes are phenomena described as a transiently enhanced brightness in a limited area of the visual field, halos, image distortion (strobo-pleurogenic, or pleuro-ophthalmic effects), or colored bright lights, or multiple images (retinal persistency). Phosphophens are usually triggered by sudden variations in light intensity. Corlanor can cause phosphophens, thought to be mediated through an abnormal retinal response to photoreceptors [see Clinical Pharmacology (12.1)]. Onset is generally within the first 2 months of treatment, after which they may occur repeatedly. Phosphophens were generally reported to be of mild to moderate intensity, and to treatment discontinuation in < 1% of patients, most resolved during or after treatment.

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Corlanor® (ivabradine)

Manufactured for: Amgen Inc.

One Amgen Center Drive

Thousand Oaks, California 91320-1799

Patent: http://pat.amgen.com/Corlanor/
The Arrival of HS-Troponin Assays

Practical Advice for Clinicians

Measurement of troponin has become a highly sensitive issue in the last few years. While we don’t have an assay approved yet in the United States, approval may come later this year or next year. So what should physicians expect when measuring highly sensitive troponin? A recent issue of JACC discusses this issue in an article titled “Implications of Introducing High-Sensitivity Cardiac Troponin T Into Clinical Practice.” Providing some practical advice based on this publication is James Januzzi, Jr., MD, the Roman DeSanctis Scholar, Clinical Scholar, and also a Professor of Medicine at Harvard, as well as the Scholar at the Massachusetts General Hospital.

CardioSource WorldNews: Let’s begin by talking about SWEDEHEART. Can you give us some background on it?

Dr. Januzzi: The SWEDEHEART Registry is an interesting and very large data set. Basically, in the country of Sweden, there is a centralized data repository that can track the course of over 40,000 patients admitted to the hospital for various diagnoses. We just published a paper in JACC Heart Failure, for example, looking at the experience from SWEDEHEART with heart failure patients. In the JACC study, the authors used the SWEDEHEART Registry to look at patients admitted to the intensive care unit or similar setting for suspected acute coronary syndrome.

Now, what did they find in terms of the data? Well, I think it’s important to emphasize that the idea behind the study was to ask the question. What has been the practice patterns around these patients, the final diagnoses of these patients, as well as the prognosis of the patients, because there’s still some open questions about what highly sensitive troponin will bring.

What the authors found was that a substantial percentage of patients had very low values for highly sensitive troponin. Interestingly, in this study, some have previously suggested that patients with very low values—in other words, those below the detection limit of the assay—could potentially be rapidly triaged, because they’re unlikely to have acute myocardial infarction (MI) or unstable angina. What they actually found in SWEDEHEART data was that that wasn’t the case; there was a measurable number of patients with very low, highly sensitive values that, indeed, had an acute coronary syndrome. So that’s an important point.

On the other hand, the spectrum, they found, as has been shown, that highly sensitive troponin reclassifies patients from unstable angina pectoris to acute MI in about 20% of cases. The newer troponins are more sensitive than the older ones in finding these patients, but there was a substantial number of patients that had an elevated value for highly sensitive troponin who did not have an acute MI. This proves to be a cautionary tale for clinicians when we start testing.

When I looked at this article and saw that the sub-title included some practical advice for clinicians, my immediate thought was that this could be one of the best-read pieces in JACC for the year. Seriously, this has caused a great deal of controversy and consternation. In this country what should we expect, and what practical advice can you give? Yes. It’s an incredibly important topic, because we use troponins all the time, and when we are looking at these patients the way we are carefully watching for the presence of MI, particularly because that has a defined treatment strategy. What we can tell clinicians is that, when we shift to the highly sensitive troponins, we will be able to, in a much more rapid fashion, identify or exclude necrosis of the myocardium. There are data showing that within 1 to 3 hours a patient can be successfully completed in their rule-out or rule-in; so unlike older troponin assays, the decision might be earlier, which is nice.

However, because of the increased sensitivity, we now recognize that there are situations where myocardial necrosis occurs outside of an acute MI that we never detected before.

In this editorial, I provided a figure from the universal definition of MI Task Force Document that really illustrates how clinicians should be thinking about troponins. They’re no longer to be thought of as a heart attack biomarker. They should be thought of as a myocardial injury biomarker. So situations like myocarditis, hypertension, heart failure—things that are not heart myocardial infarction per se—will be picked up with these assays. But another very important point for clinicians to recognize is that the SWEDEHEART investigators found that regardless of gender or age, if the highly sensitive troponin is elevated the risk for the patient was higher. Almost truly independent of the diagnosis patients didn’t have to have an MI. If the highly sensitive troponin was high the patient’s risk was considerably higher, which really says that we need to pay attention to why the troponin is abnormal and not just say, “Ah, it’s not an MI. Let’s just discard that elevated value.”

I know a lot of centers have been trying to get people processed in and out faster and faster. This finding will really be helpful to patients as they will know sooner and not have to wait hours for some determination.

We know—and again, we have the benefit of knowing from the European experience—that one may be able to successfully complete the process of ruling in or ruling out within just a few hours. The data for highly sensitive troponin show that patients are more often than not positive at presentation, and soon after presentation. One recent study, called the TRAPID-AMI Study, showed that within 1 hour you can see a significant delta, a significant rise in those patients destined to have an MI. So, by using a rapid rule-out or rule-in strategy, three-quarters of patients can have a disposition within an hour.

That’s got to remove some stress from the patient, because it’s not a happy thing to be in the hospital in the first place if you’re wondering whether you had a heart attack.

Certainly not. And it also adds a lot of relief to the emergency department setting in terms of making decisions, whether a patient should or should not be triaged in or out.

I think, if anything, the initial reaction from cardiologists will be somewhat of concern, maybe frustration, because now we can see things that we hadn’t seen before. However, you talk to the Europeans and they say, “Do not take this away from us. We love it. We’ve learned a lot, and we’ve changed our practice styles because we now can detect things that we weren’t able to before.” That can only improve care in the end.

So, coming soon to a United States near you?

Yes. Absolutely.
Cardiologists, department managers, and system executives have a bevy of data at their fingertips—from congestive HF readmission rates to the most recent EKG reading for the next office visit. The challenge is not an inadequate amount of available data, but rather having the right health information at the right time in order to deliver optimal care. How effectively data is managed, shared, and utilized across the care continuum is a clear indication of how informed an organization truly is. This column is the next installment in a series outlining the five core attributes of a value-based enterprise. In combination with being integrated, scaled, rationalized, and responsive, being an informed organization is essential for successfully transitioning to a value-based environment.

The Right Information at Every Level
Health systems and the cardiologists they support have more information available to them than ever before, but more data is not, in many cases, synonymous with the right data. Gorging on data or, conversely, failing to take advantage of pertinent and readily available data leads to wasted opportunities, ineffective processes, and uninform ed decision-making. Informed organizations have a keen awareness of what they need to know now and in the future, while possessing the infrastructure to acquire and manage the continuous flow of information. They also have a clear vision for converting relevant data into actionable information. Pertinent health information needs to be made available to physicians at the point of care and administrative information is needed at the system level to make critical organizational decisions—and there are several levels in between.

To simplify, let’s take a look at some examples of why having the right information at the right time is pivotal in supporting patient care, business operations, and service line strategy.

• **Supporting Patient Care** – I’ve had numerous conversations with cardiologists around the topic of care coordination and continuity, and the information that’s necessary to achieve this. For instance, cardiologists repeatedly tell me that when it comes to post-acute care follow-up visits, they want the discharge summary, EKG, and list of relevant medications from the hospital, and that this information be readily accessible in their electronic health records. Instead, they’re spending considerable time sifting through the patient’s medical record and discerning the pertinent information from the “noise.” Additionally, information now comes from a cornucopia of sources (i.e., devices, other providers, patients, and patients’ families), making the management and sharing of data ever more complicated, yet ever more urgent. Informed organizations support physicians’ ability to deliver optimal care by putting the processes and systems in place that provide them timely information where they need it.

• **Supporting Business Operations** – Moving from clinical decisions to department operations, the goal of gathering and analyzing data revolves around evaluating operational performance. This data should align with the specific information needs of practice and/or department managers. For example, dashboards have become a common vehicle for presenting data—often related to patient satisfaction, revenue cycle, quality elements, staffing efficiency, and operating costs—in a visually compelling and digestible way. However, many dashboards today look like airplane cockpits. Instead of simplifying and distilling the information needed, the amount of data, indicators, and targets tend to camouflage the most salient statistics operations managers need to make key business decisions. For data to become information that produces operational improvements, it must first be manageable. Instead of a cockpit, operational dashboards should more closely resemble the dashboard of your car, clearly highlighting the 3-5 most relevant statistics or performance indicators.

• **Supporting Service Line Strategy** – As we elevate the discussion to the system level, informed organizations and leaders are better positioned to develop immediate and long-term strategic plans and effectively execute these plans. Health systems are under intensifying pressure to possess the knowledge necessary to acclimate to payment reform and the transition to value, as well as integrate services across the care continuum. Attempting to meet these demands without the appropriate intelligence and a clearly defined strategy for doing so will bury an organization. Service line growth, as well as physician recruitment and retention, are prominent goals in the strategic plans of many organizations.

Thus, improving access to health services is a priority for organizations as they look to increase their patient population and market position. In designing strategies to expand geographic reach and patient access, for example, some sophisticated organizations are doing ZIP code and utilization analyses to assess how far patients are traveling to receive certain clinical services. This information is then being used to design strategies for reaching underserved populations, such as telemedicine programs, without having to build a physical office or convince providers to travel to distant locations.

A Complex, Crucial Pursuit
Being informed is a foundational attribute for a thriving value-based enterprise. From a high-level understanding of drastic shifts in the payment environment to a strong grasp on local market dynamics to the utilization of organization and patient-specific data sources, cultivating and maintaining an informed organization is no small feat. But it is a crucial one. In order to successfully make the transition to a value-based environment, it’s essential that organizations recognize and respond to the need to provide physicians, department and practice managers, and system leadership with the right information at the right time and in the right place.

Nathan McCarthy is a senior manager at ECG Management Consultants, Inc.
Lack of accessibility to health care is often evaluated as a measure of bias. There is a committee on access of care in the New York State Cardiac Advisory Board. Reports on the availability of cardiac services to the underserved population are a concern there and across the country as it applies to minorities and women. But what about the uninsured?

I recently attended a regional American Heart Association (AHA) board meeting in Atlanta, GA, and the topic turned, as it often does, to efforts to reduce cardiovascular risk. There are programs on healthy school lunch choices, blood pressure screening programs, smoking cessation initiatives, and so forth. In recent years, cardiologists have not been engaged in a major way with the AHA on the local level except in fundraising events. The major lobbying of this venerable health advocacy organization has been the job of lay volunteers—many of whom are patients—and the AHA staff. In these meetings we often discuss, in addition to fundraising, programs to reduce cardiovascular risk on a population basis. Many of the initiatives are driven by what is perceived to be possible in the political climate. My state of Georgia has one of the lowest cigarette tax rates in the country, and yet it has, until now, been impossible to get a bill passed in the legislature to increase it. The AHA backed off its initiatives, waiting for a future opportunity to push for this well-known deterrent to smoking, especially by young people.

It occurs to me that there is another public health issue that could impact cardiovascular health: the accessibility of health care. I am not talking about how many cardiac surgeries or percutaneous intervention programs are nearby, but the population’s ability to actually see doctors. Doctors are great sources of information on the prevention and treatment of disease. The problem is that many people never consult a doctor because it costs a lot of money and, without insurance, the cost is even greater. So, if access to doctors is a contributor to improved cardiovascular health, why aren’t doctors pushing to make this more available? We, as cardiologists, are mostly members of the American College of Cardiology (ACC), an organization that is on record as supporting universal health care. But neither the AHA nor the ACC can legislate the expansion of health care coverage. This falls to state legislatures who have, in many cases, refused to expand Medicaid coverage to enable better access, even though, to the states, it is largely free money.

There is now evidence that the states that have enabled more of their citizens to have health coverage have had significantly more patients with diabetes diagnosed and started on treatment. I suspect the same is true for hypertension. States that have accepted the funds for Medicaid expansion have been able to keep hospitals caring for the poor, including many working poor, to remain open. I learned at the AHA meeting that five rural hospitals in Georgia have recently closed and others are soon to do so because of lack of funding. Doctors are needed in low-income, rural areas, but without patients willing or able to pay for services, these areas go without doctors. Recently, 22,000 physicians signed a petition to abolish the maintenance of competence requirements of the American Board of Internal Medicine because it is ineffective and costly for doctors. Surely the doctors and the advocacy lay organizations could apply pressure to assure that access to health care and prevention is available to all. It is, after all, effective and supportive of doctors and hospitals. Tell the states that have not expanded Medicaid coverage, “Take the money!”

There is another public health issue that could impact cardiovascular health: the accessibility of health care.
COMING SOON

Praxbind®
(idarucizumab)
Antibodies are the body’s natural defense against pathogens. But in the last 30 years, scientists have leveraged their knowledge of immunology, microbiology, and recombinant DNA technology to create man-made antibodies to fight numerous diseases. These therapeutic monoclonal antibodies (mAbs) can interrupt disease pathology on a molecular level by blocking receptors or interfering with cell-to-cell transmission. Recent developments in antibody technologies have gone beyond immunology-related therapies to non-immune–modulating treatments.

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**A New Era in Healthcare**

Powerful new technologies have been a key to progress in mAb development. Sanofi/Regeneron are utilizing the unique VelocImmune™ mouse technology in which mouse DNA that codes for immune system proteins has been genetically-engineered to produce human DNA instead. With this technology it is possible to rapidly and efficiently generate fully human therapeutic antibodies that may benefit the health of millions of people in ways unforeseen even a few decades ago.

Over 500 therapeutic antibodies are in development in a variety of categories

**References:**


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