**RESEARCH LETTER**

Quality Assessment of 7 Cardiovascular Drugs in 10 Sub-Saharan Countries: The SEVEN Study

Substandard and falsified medicines pose a serious threat to patient safety and public health.1 Studies on the quality of drugs have focused mainly on antimicrobial agents, such as antiretroviral therapy (for human immunodeficiency virus) and antimalarial medications.2 Although cardiovascular disease kills millions of Africans,3 to our knowledge, little published research has explored the quality of essential cardiovascular disease medicines to date. We therefore performed a quality assessment of 7 commonly used cardiac drugs (ie, an anticoagulant drug, a statin, and 5 antihypertensive drugs) in 10 countries of sub-Saharan Africa.

**Method** | We assessed 7 of the most common cardiovascular medicines used in Africa: the anticoagulant acenocoumarol, the statin simvastatin, and 5 antihypertensive drugs, including furosemide, hydrochlorothiazide (a diuretic), captopril (an angiotensin-converting enzyme inhibitor), atenolol (a β-blocker), and amlodipine (a calcium channel blocker).

According to Medicine Quality Assessment Reporting Guidelines,4 we prospectively collected samples using standardized methods between November 2012 and August 2014 from pharmacies and street markets in 10 African countries, including Benin, Burkina Faso, Congo-Brazzaville, Côte D’Ivoire, Guinea, Mauritania, Niger, the Democratic Republic of the Congo, Senegal, and Togo.

A falsified medicine is one which is deliberately and fraudulently mislabeled. Falsified drugs may contain different ingredients (both harmless and toxic) from the one stated on the label or a different content of the expected active ingredient. Substandard medicines are those produced by legitimate manufacturers that do not meet required quality specifications. We did not conduct forensic analyses of the drugs to determine whether they were substandard or falsified drugs.

A reversed-phase liquid chromatography with tandem mass spectrometry method was developed5 in a certified public laboratory in Paris, France, to accurately quantify the active ingredient. Three quality categories were defined based on the ratio of measured to expected dose of the active ingredient in the sample; a ratio of 95% to 105% indicated good quality, a ratio of 85% to less than 95% or greater than 105% to 115% indicated low quality, and a ratio less than 85% or greater than 115% indicated very low quality. Overall, drugs were considered to be of poor quality if they were low or very low quality.

**Results** | According to the sampling protocol, 3468 samples were collected and 1530 were tested at random, of which 249 (16.3%) were deemed to be of poor quality. The prevalence of poor-quality drugs differed significantly between drugs (P < .001), with the lowest prevalence for acenocoumarol (0 of 165 samples [0%]) and highest for amlodipine (87 of 305 samples [28.5%]), and between countries, although this difference did not reach statistical significance (P = 0.08) (Table). The proportion of poor-quality drugs exceeded 20% in Benin, Congo-Brazzaville, Niger, and the Democratic Republic of the Congo and was below 10% in Guinea, Senegal, and Togo (Figure). While low-quality samples were observed in all 10 countries, very-low-quality samples were obtained only from Niger (1 of 100 samples [1.0%]), Côte D’Ivoire (3 of 295 samples [1.0%]),

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### Table. Percentage of Poor-Quality Drugs by Drug and by Country of Purchase

<table>
<thead>
<tr>
<th>Drug</th>
<th>Benin (0/165)</th>
<th>Burkina Faso (0/165)</th>
<th>Congo-Brazzaville (0/165)</th>
<th>Côte D’Ivoire (0/165)</th>
<th>DRC (0/165)</th>
<th>Guinea (0/165)</th>
<th>Mauritania (0/165)</th>
<th>Niger (0/165)</th>
<th>Senegal (0/165)</th>
<th>Togo (0/165)</th>
<th>Total (0/165)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acenocoumarol</td>
<td>0/50</td>
<td>0/10</td>
<td>0/20</td>
<td>0/25</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/165</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>20/50 (40.0)</td>
<td>0/10</td>
<td>17/30 (56.7)</td>
<td>28/75 (37.3)</td>
<td>10/20 (50.0)</td>
<td>0/10</td>
<td>4/40 (10.0)</td>
<td>1/30</td>
<td>0/20</td>
<td>7/20 (35.0)</td>
<td>87/305 (28.5)</td>
</tr>
<tr>
<td>Atenolol</td>
<td>13/30 (43.3)</td>
<td>6/30 (20.0)</td>
<td>6/30 (20.0)</td>
<td>7/45 (15.6)</td>
<td>4/10 (40.0)</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>1/20</td>
<td>0/20</td>
<td>37/245 (15.1)</td>
</tr>
<tr>
<td>Captopril</td>
<td>15/30 (50.0)</td>
<td>0/20</td>
<td>10/20 (50.0)</td>
<td>12/45 (26.7)</td>
<td>0/10 (0)</td>
<td>2/10 (20.0)</td>
<td>9/30 (30.0)</td>
<td>10/10</td>
<td>0/20</td>
<td>2/20 (10.0)</td>
<td>60/235 (25.2)</td>
</tr>
<tr>
<td>Furosemide</td>
<td>13/45 (28.9)</td>
<td>8/40 (20.0)</td>
<td>0/20</td>
<td>1/45 (2.2)</td>
<td>5/20 (25.0)</td>
<td>NA</td>
<td>3/20 (15.0)</td>
<td>0/20</td>
<td>0/20</td>
<td>0/20</td>
<td>30/240 (12.5)</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>3/40 (7.5)</td>
<td>0/20</td>
<td>0/20</td>
<td>0/10 (0)</td>
<td>0/10 (0)</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>0/10</td>
<td>3/160 (1.9)</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>3/50 (6.0)</td>
<td>0/20</td>
<td>0/10</td>
<td>4/50 (8.0)</td>
<td>5/10 (50.0)</td>
<td>NA</td>
<td>10/20 (50.0)</td>
<td>10/10</td>
<td>0/20</td>
<td>NA</td>
<td>32/180 (17.6)</td>
</tr>
<tr>
<td>Total</td>
<td>67/125 (20.6)</td>
<td>14/140 (10.0)</td>
<td>33/150 (22.0)</td>
<td>52/295 (17.6)</td>
<td>24/90 (26.7)</td>
<td>2/50 (4.0)</td>
<td>23/150 (15.3)</td>
<td>24/100</td>
<td>1/130</td>
<td>9/100</td>
<td>249/1530 (16.3)</td>
</tr>
</tbody>
</table>

Abbreviations: DRC, Democratic Republic of the Congo; NA, not applicable.
Benin (10 of 325 samples [3.1%]), and Congo-Brazzaville (10 of 150 samples [6.7%]).

Discussion | To our knowledge, we have presented the first data on the quality of cardiovascular drugs in countries in sub-Saharan Africa. We found a high prevalence of poor-quality drugs, with a little less than 1 in 6 samples failing to meet standards.

The observed variation in quality by country merits consideration. Indeed, in 2013, operation BIYELA was carried out in 23 African countries and resulted in the interception of more than 500 million illicit or falsified drugs, most of which were from Benin, Tanzania, and the Democratic Republic of the Congo.6

Conclusions | A combination of political apathy and corruption may make the task of improving the quality of drugs especially challenging in the developing world. Increasing public awareness and heightening international scrutiny are necessary to bring about changes. Improving the quality of cardiovascular drugs would be a major achievement for the prevention and control of noncommunicable diseases in sub-Saharan Africa. Improvement in the public’s access to effective medications also remains an important goal that will help to achieve the target of the United Nations of a 25% reduction in premature cardiovascular disease mortality by 2025.7 Accessibility to quality drug testing for interested parties is a crucial requirement.

Marie Antignac, PharmD, PhD
Bara Ibrahima Diop, MD
Bernard Do, PharmD, PhD
Roland N’Guetta, MD
Ibrahim Ali Toure, MD
Patrick Zabsonre, MD
Xavier Jouven, MD, PhD

Author Affiliations: Department of Pharmacy, Saint-Antoine Hospital, East Paris University Hospitals, AP-HP, Paris, France (Antignac); Cardiology Department, University Hospital Fann, Dakar, Senegal (Diop); Department of Laboratories, General Agency of Health Equipment and Products, AP-HP, Paris, France (Do); Faculty of Pharmacy, University of Paris-Sud, UA 401, Chatenay-Malabry, France (Do); Cardiology Department, Cardiology Institute of Abidjan, Abidjan, Côte d’Ivoire (N’Guetta); Internal Medicine and Cardiology Department, Lamorédé National Hospital, Abidou Moumouni University, Niamey, Niger (Toure); Cardiology Department, National Hospital of Sanou Souro of Bobo Dioulasso, Ouagadougou, Burkina Faso (Zabsonre); Department of Cardiology, European Georges Pompidou Hospital, AP-HP, Paris, France (Jouven); INSERM U970, Paris, France (Jouven); Paris Descartes University, Paris, France (Jouven).

Corresponding Author: Marie Antignac, PharmD, PhD, Department of Pharmacy, Saint-Antoine Hospital, East Paris University Hospitals, AP-HP, 184 Rue du Faubourg Saint-Antoine, Paris, France 75012 (marie.antignac@aphp.fr).

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Study concept and design: Antignac, Diop, Jouven.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Antignac, Jouven.

Critical revision of the manuscript for important intellectual content: Antignac, Jouven.

Statistical analysis: Antignac, Jouven.

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Study supervision: Antignac, Diop, N’Guetta, Jouven.

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Editor’s Note
Evaluating and Improving the Cardiovascular Drug Supply for Better Global Health

The World Health Organization and its member states have agreed to the ambitious goal of reducing the risk of premature mortality from noncommunicable diseases, including heart disease and stroke, by 25% by 2025. This voluntary goal includes a national health system response target of “80% availability of the affordable basic technologies and essential medicines, including generics, required to treat major noncommunicable diseases in both public and private facilities.”1 A 2012 United Nations report2 estimated that essential medicines were available in 52% and 68% of public and private pharmacies, respectively, between 2007 and 2011, which demonstrates this availability gap. While this health system response target assumes that the available medicines will contain the active pharmaceutical ingredient at the stated level, data from some studies, such as those focused on malaria,3 suggest that these drugs fail chemical analysis in up to one-third of samples and thus may not achieve disease prevention and control.

In this issue of JAMA Cardiology, Antignac et al4 take an important initial step toward evaluating the medicine quality of common drugs used for cardiovascular disease prevention and control in 10 sub-Saharan African countries using standardized methods from 2012 to 2014. The authors use high-quality reversed-phase liquid chromatography with tandem mass spectrometry, which is a sophisticated, relatively expensive, and reliable method. Cheaper, field-based, real-time methods to evaluate drug quality, such as the Global Pharma Health Fund Minilab or other similar platforms, will likely be even more useful for larger-scale efforts in the future. The authors use strict thresholds to define poor drug quality that some may debate, but their overall findings emphasize the scope and importance of drug safety not only in sub-Saharan Africa but all around the world, particularly in an era of globalized drug manufacturing and distribution in the absence of any global law or treaty against medicine crime. Drugs on national and global essential medicines lists, including the medicines evaluated by Antignac et al, represent priority medicines for surveillance.

To improve drug quality, the World Health Organization has created a Global Surveillance and Monitoring System for substandard, spurious, falsely labeled, falsified, and counterfeit medical products, which was launched in western Africa in 2013 following the development of the African Medicines Regulatory Harmonization Initiative in 2009. The World Health Organization provides technical support, including training, to member states for addressing suspected medical products while facilitating international collaboration among national focal points. This network seeks national-level reporting on regulatory capacity, international collaboration, and identification of major needs and challenges and will report its findings to the World Health Assembly in 2017. Improving and maintaining the safety of the global medicine supply is a shared priority for many stakeholders, including patients, physicians, governments, and payers as well as legitimate pharmaceutical manufacturers, who all benefit from a safe and effective medicine supply chain. To my knowledge, most reports have focused on drugs for communicable diseases to date. Data from Antignac et al highlight the growing importance of access to safe, essential medicines for preventing and controlling the leading causes of global deaths, namely heart disease and stroke, to achieve the “25×25” goal.

Mark D. Huffman, MD, MPH

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Left Ventricular Dysfunction and Conduction Disturbances in Patients With Myotonic Muscular Dystrophy Type I and II

Electrocardiographic (ECG) abnormalities and left ventricular (LV) dysfunction are associated with mortality in type I and type II myotonic muscular dystrophy (MMD).1-3 We sought to quantitate the baseline prevalence and longitudinal incidence of conduction abnormalities and LV dysfunction during intermediate-term follow-up of a cohort of patients with MMD.

Methods | The source cohort is a Johns Hopkins Hospital institutional review board–approved prospective open cohort of consecutive patients with MMD referred to the Electrophysiology Service. The cohort was divided into 2 sections. Those with magnetic resonance imaging and/or additional genetic testing provided written informed consent. However, those who did not undergo testing beyond our clinical routine were enrolled in a deidentified consent-exempt registry. We retrospectively summarized data on 136 patients with MMD-I and 28 patients with MMD-II with genetically confirmed diagnosis and baseline ECG between January 1997 and August 2014. Of all patients, 124 (76%) were unrelated, 12 patients (7%) belonged to 4 separate families (3 individuals per family), and 28 patients (17%) belonged to 14 separate families (2 individuals per family). After exclusion of ECGs with only paced or non-