

Communicable disease-related sudden death in the 21st century in Nigeria

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Background: Some cases of sudden death (SD) have been attributed to communicable diseases (CD) in middle- and low-income countries of the world even in this 21st century. CDs produce clinical symptoms and signs over several days before culminating in death. They are also amenable to treatment with antimicrobials if affected persons present early. We sought to find out the incidence of CD-related SD at the Ladoke Akintola University of Technology Teaching Hospital (Osogbo, Osun State, Nigeria) – a tertiary health facility in southwest Nigeria – and the prevailing associated factors.

Methods: We conducted a retrospective study of CD-related SD in adult patients aged 18 years and older that occurred from January 2003 to December 2011. The Statistical Package for the Social Sciences version 16 was used for analysis of the generated data. Percentages and frequencies were calculated.

Results: There were 17 (39.6%) CD-related SDs out of the 48 cases of SD studied. CD-related SD also accounted for 2.4% of all adult medical admissions. The mean age of the patients was 37.6 ± 11.6 years, age range of 25–62 years, mode of 25 years, and median 34 years. The male-to-female ratio was 1.8:1. Typhoid sepsis was responsible for SD in 47.1% of patients, pulmonary tuberculosis in 17.7% of patients, and lobar pneumonia in 17.7% of patients. The most affected age group was the 20–29-year-old group (41.2%), while the unskilled occupational group was the most affected occupational group with 35.3% of them having SD. Most of the patients with acute bacterial infection died of multiple organ failure.

Conclusion: There is an urgent need to step up public health strategies to curtail infections in this environment, encourage better use of the existing health facilities by the people, and the government should strive hard to make health a top priority.

Keywords: infections, septic shock, typhoid sepsis, pulmonary tuberculosis, HIV/AIDS, public health

Introduction

Sub-Saharan Africa (SSA) has been under the scourge of communicable diseases (CDs) for a long period of time, and sudden deaths (SDs) are still responsible for most of the morbidity and mortality in the region. CDs continue to be a burden although the non-CDs (NCDs) are now coming up as an equally burdensome disease, thus leading to a double burden on the health care services and economy of this resource-poor region.¹

The World Health Organization (WHO) defines SD as death occurring within 24 hours of an abrupt change in one's previous clinical status.² SD refers to nonviolent, nontraumatic deaths, but studies have shown that psychologically and physically traumatic events can precipitate SD.^{3,4}

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NCDs have been incriminated as the principal culprits in SD, but some deaths that occur out of hospital or within 24 hours of admission in our hospitals are caused by CDs, and as such, these CDs are pooled into the category of SDs. The most common cause of death worldwide now is cardiovascular disease;⁵ this is similar for SD.⁶

Before 1900, the world was in the first stage of epidemiologic transition, which is the stage of pestilence and famine, with infectious diseases and malnutrition emerging as the predominant causes of death; improvement in public health and nutrition has led to the emergence of the second stage of the epidemiologic transition known as the stage of receding pandemics, with concomitant decline in death rates due to malnutrition and infections.⁵ The second stage of epidemiologic transition includes hypertension, coronary heart disease, stroke (predominantly hemorrhagic), amongst others.⁵ A study in Saudi Arabia reported that the cause of SD in 45 (20.2%) out of 223 cases was due to infectious diseases.⁷ CDs on their own usually present with signs and symptoms, which often continue to worsen over days if left untreated, are poorly treated, or if the correct diagnosis is missed altogether, before finally leading to death.

In view of the fact that CDs are easily amenable to treatment once sufferers present early, prompt diagnosis is made and appropriate treatment is instituted, patients with CD should therefore not present with SD, we therefore consider it important to conduct this retrospective study to find out the proportion of such cases that are presenting as SD. We are of the opinion that a study of this nature will help in mounting a public health campaign against the actions and inactions of our people that are making diseases, which can be easily cured with prompt and adequate antimicrobial treatment, the cause of SD in the 21st century.

Methods

We conducted a retrospective study of SD caused by CDs in adult patients aged 18 years and older, carried out at the Ladoke Akintola University of Technology Teaching Hospital (LAUTECH), Osogbo, Osun State, southwest Nigeria. We retrieved the case notes of all the cases coded as sudden unexpected death from nonviolent, nontraumatic causes that occurred from January 2003 to December 2011. These hospital records were comprised of cases indicating that there was unexpected death before arrival in the hospital and death within 24 hours of admission to the hospital. We then sorted out the subset of cases where the postmortem diagnosis was classified as CD. Further information was subsequently obtained from the patients' case notes and

autopsy reports pertaining to demographic data, symptoms on presentation, investigations done, and clinical diagnosis. The diagnosis of the patients was based on the cytopathology reported at autopsy. Ethical clearance was obtained from the Research Ethical Committee of LAUTECH. Data entry was inputted into the computer using the Statistical Package for Social Sciences version 16 (IBM Corporation, Armonk, NY, USA) for statistical analysis. Frequencies and percentages were calculated.

Results

There were 48 cases of SD in the period spanning January 2003 and December 2011, inclusive. A subset of 17 (35.5%) of the SD cases were caused by CDs, with NCDs accounting for 29 (60.4%) of patients, while immunosuppressive disease and chronic undernutrition accounted for two (4.2%) patients. These aforementioned 17 cases were analyzed to get more information on the CD-related SD.

The overall adult mortality of medical patients in the hospital during this period of study was 25.5% (718 out of a total admission of 2,821 patients). The total admission included all cases of death before arrival at the hospital that had autopsy done on them. The CD-related SD accounted for 2.4% (17/718) of all adult medical mortality and 0.6% (17/2,821) of all adult medical admissions.

Table 1 shows the sociodemographic characteristics of the patients with CD as the cause of their SD. The mean age of the patients was 37.6 ± 11.6 years, age range of 25–62 years, mode of 25 years, and a median of 34.0 years. The male-to-female ratio is 1.8:1.

Table 1 Sociodemographic characteristics

Characteristics	Number of patients	%	Remark
Age group (years)			
20–29	7	41.2	
30–39	2	11.8	
40–49	5	29.4	
50–59	2	11.8	
≥60	1	5.9	
Gender			
Male	11	64.7	
Female	6	35.3	
Occupation			
Unskilled	6	35.3	PT, PWT, CL, D
Skilled	1	5.9	Bricklayer
Professional	4	23.5	Police officer, contractor
Student	3	17.7	
Not stated	3	17.7	

Abbreviations: PT, petty trader; PWT, palm wine tapper; CL, casual laborer; D, drummer.

Table 2 Postmortem diagnosis in the patients with communicable disease-related sudden death

PM diagnosis	Number of patients	%	Remark
Typhoid sepsis	8	47.1	
LP + sepsis	3	17.7	One had a huge obstructed incisional hernia
Cerebral abscess + ICP	1	5.9	
PTB	3	17.7	
Respiratory failure	1	5.9	
SH + HS	2	11.8	
HS + sepsis + metastatic abscesses	1	5.9	
Septic shock	1	5.9	Complicating septicemia

Abbreviations: PM, postmortem; LP, lobar pneumonia; ICP, increased intracranial pressure; PTB, pulmonary tuberculosis; SH, severe hemoptysis; HS, hemorrhagic shock.

Table 2 shows the details of patients with a postmortem diagnosis of CD as the cause of their SD, while Table 3 shows the postmortem diagnosis according to age group. However, there were two patients who did not fit into the group of CD-related SD that are worthy of mentioning. One was a 32-year-old female trader with severe immunosuppressive disease, and the other was a 60-year-old male security guard with chronic under-nutrition, who also had features of poor personal hygiene and neglect, but no evidence of natural disease or marks of violence.

There were no symptoms recorded for 14 (82.4%) of the patients who were brought in dead. The rest (17.7%) consisted of the two patients with pulmonary tuberculosis (PTB) and severe hemoptysis who died of hemorrhagic shock. In addition, a 62-year-old female patient with lobar pneumonia, septicemia, and a huge obstructed incisional hernia presented with a 5 day history of cough and catarrh. She also had clinical evidence of a chest infection with septic shock; she died within a few minutes of admission.

Discussion

In the 19th century, the world witnessed the first stage of an epidemiologic transition known as the stage of pestilence and famine, with infectious diseases and malnutrition emerging as the most common causes of death;⁵ however, improvement in public health and nutrition has led to the emergence of the second stage of the epidemiologic transition known as the stage of receding pandemics, with accompanying decline in death rates due to malnutrition and infections.⁵ The second stage of the epidemiologic transition includes hypertension, coronary heart disease, and stroke (predominantly

Table 3 Postmortem diagnosis according to age group in patients with communicable disease-related sudden death

Age group (years)	PM diagnosis	Number of patients (%)	Remark
20–29		7	Total number of patients
	Typhoid sepsis	4 (57.1)	
	PTB	1 (14.3)	Severe hemoptysis
	LP + sepsis	1 (14.3)	
30–39	HS + sepsis	1 (14.3)	Metastatic abscesses
		2	Total number of patients
	Cerebral abscess + ICP	1 (50.0)	
	Typhoid sepsis	1 (50.0)	
40–49		5	Total number of patients
	PTB	2 (40.0)	
	SH + HS	1 (20.0)	
	Respiratory failure	1 (20.0)	
50–59	Typhoid sepsis	2 (40.0)	
	Septic shock	1 (20.0)	Complicating septicemia
		2	Total number of patients
	Typhoid sepsis	1 (50.0)	
≥60	LP + septic shock	1 (50.0)	
		1	Total number of patients
	LP + sepsis	1 (100.0)	+ huge obstructed incisional hernia

Abbreviations: PM, postmortem; PTB, pulmonary tuberculosis; LP, lobar pneumonia; HS, hemorrhagic shock; ICP, increased intracranial pressure; SH, severe hemoptysis.

hemorrhagic), amongst others.⁵ SSA (Nigeria inclusive) is not left out of this epidemiologic transition, but it is also still battling with CDs due to poverty, ignorance, misplaced priorities, and widespread corruption. This has paved the way for CD-related SD to still be rearing its ugly head in our communities.

In this study, CD-related SD accounted for 2.4% of all adult medical deaths and 0.6% of all adult medical admissions. This study further showed that 35.5% of SD was caused by CDs, and typhoid sepsis accounted for 47.1% of SD as shown in Table 2, which was the most common amongst the CDs. The proportion of SD caused by CD (35.5%) in this study is higher than the 20.2% reported for infections in the Saudi Arabia study, which also reported lobar pneumonia separately as being responsible for 13.0% of SDs, hence resulting in a total of 33.3% SDs, which supports our finding from this study.⁷ Lobar pneumonia alone accounted for 17.7% of the CD-related SD, which is also close to the percentage quoted in the Saudi Arabia study.⁷ All of the patients who had acute

bacterial infection had septic shock and died on account of multiple organ failure. It is our view that a delay in seeking a prompt diagnosis and appropriate treatment, on the part of the patients, led to the so-called “SD.”

Similarly, PTB was also responsible for 17.7% of the CD-related SD with two of the infected patients dying of hemorrhagic shock following massive hemoptysis, and the third patient died of respiratory failure. The case of a 60-year-old immigrant worker in New York who died suddenly is a good illustration of this. Investigation into the cause of his death revealed that he had been coughing for months before his death, and that PTB was the cause of his death; in addition, he had infected a good number of his coworkers.⁸ In another study of SD in suspicious circumstances in two young subjects, the cause of death at postmortem was found to be tuberculosis.⁹ PTB is a chronic infectious disease that would be present for 1 month or longer. PTB is one of the most common causes of massive hemoptysis; a study that reviewed 123 cases of massive hemoptysis confirmed that 38.2% of patients had PTB, closely followed by 30.1% with bronchiectasis.¹⁰ Massive hemoptysis is unpredictable, and eight apparently clinically stable patients died suddenly while awaiting surgery or endoscopy in the same review.¹⁰ The human immunodeficiency virus (HIV) epidemic has greatly increased the number of cases of active tuberculosis per capita in SSA to the extent that the region now has the highest rate.¹¹ The patients with PTB in this study were not tested for HIV at autopsy.

The mean age of the patients in this study was 37.6 ± 11.6 years, with a mode of 25 years, median of 34 years, and an age range of 25–62 years. The Saudi Arabia study showed that the greatest incidence of SD occurred at the extremes of life (<12 months and >60 years).⁷ Our study did not show this because our focus was on adults, so the pediatric age group was excluded from our study. We also did not notice this high incidence in the elderly adults, as the young adults and middle-aged subjects (aged 20–59 years) constituted 94.2% (Table 1) of those who had SD secondary to CDs. The most affected age group was the 20–29-year-old age group at 41.2%, followed by the age group of 40–49-year-olds at a rate of 29.4%. Patients with an age <40 years accounted for 53.0%, while those in <50 years accounted for 82.4% of the CD-related SD. A study of SD in Cape Town, South Africa showed that infections were responsible for most of the deaths (26.1%) in the youngest age group (18–29 years).¹² In this age group, 13.6% of patients died of pneumonia, while 12.5% of them died of meningitis; PTB was common in all the age groups.¹² In a similar study in

India, SD in the young showed that infections accounted for 54.6% of deaths.¹³

There was male preponderance, with a male-to-female ratio of 1.8:1. This is in keeping with the study in India, which also showed a male preponderance, with SD mainly occurring in the age group of 30–35-year-olds.¹³ This could be because the males are the breadwinners and they could not afford to stay away from work despite ill health; hence, they kept working while ill. They are also likely to eat at work (outside their homes) most times, thereby contracting food- and water-borne infections easily. It could also be because they considered going to queue in the hospital for treatment as a waste of time.

All the occupational groups were affected, but the unskilled group took the lead in SDs, with 35.3% of the deaths occurring among this group. The low- and middle-income countries still regard infectious diseases as a major challenge due to poverty, inadequate health and sanitation infrastructure, as well as due to political upheaval.¹⁴ The unskilled occupational group are also mostly the low-income earners, and usually have a low level of education, and as such they are more vulnerable to all the problems bedeviling the low-income countries like Nigeria (where they live); hence, this high incidence of SD from CDs among this group was recorded in our study.

As mentioned earlier, typhoid sepsis accounted for 42.1% of all CDs, and it also has a high incidence rate in all the age groups, except for the ≥ 60 -year-old age group, as shown in Table 3. Typhoid sepsis is a water/food-borne disease that is endemic in developing countries like Nigeria where potable water is not readily available to a majority of the people; this is coupled with poor sanitation. Typhoid and paratyphoid fever constitute a major public health burden worldwide, especially in the developing nations.^{15,16} The global estimate of typhoid fever episodes in 2010 alone was 13.5 million, although data for this study were unavailable for seven regions including central and west SSA.¹⁶ The diagnosis of typhoid fever in SSA is difficult to make in the midst of numerous causes of febrile illnesses such as malaria.¹⁷ A Nigerian study on the rate of malaria coinfection with typhoid fever reported 0.5% coinfection rate of typhoid with malaria when diagnosis was done by blood culture, as opposed to 10.1% by a diagnosis made by the Widal test.¹⁸ In a recent study in Tanzania,¹⁹ a group of researchers found that the case definition of the WHO was better than the Widal test in diagnosing typhoid fever. The case definition of the WHO states the following.²⁰

A confirmed case of typhoid fever (fever of 38°C and >) of at least 3 days duration with *S. typhi* confirmed positive culture from any of the following samples: blood, bone marrow or bowel fluid. A probable case of typhoid on the other hand has fever with character and duration as stated for confirmed case without isolation of *S. typhi* but only has positive sero-diagnosis or antigen detection test. Chronic carrier state also occurs after an acute typhoid fever episode, with the patient excreting *S. typhi* in stools or urine (or repeated positive bile or duodenal string cultures) for more than 1 year, however some patients may be excreting *S. typhi* without a history of acute typhoid fever.

The Widal test, on the other hand, is the oldest of the agglutination tests, having been introduced in 1896 by Widal.²¹ It utilizes bacterial suspensions of *Salmonella typhi* and *S. paratyphi* “A” and “B” that have been treated to retain only the somatic lipopolysaccharide “O” antigen and the flagellar “H” antigen.^{21,22} There is an agglutination reaction between these antigens and the corresponding antibodies in the serum of patients suspected of having typhoid fever.²² The immunoglobulin M somatic “O” antibody, representing the initial serologic response of acute typhoid fever, is the first to appear, followed by the more slowly appearing but persisting immunoglobulin G flagella “H” antibody.²³ Two types of agglutination techniques are available: the slide test and the tube test.²² The slide test is a rapid screening procedure, and once the initial screening is positive, it is then done in serial dilutions of the patient’s serum to determine the strength of the antibody.²² The result is scored 0–4⁺, with 0 indicating no agglutination, 1⁺ indicating 25% agglutination, 2⁺ indicating 50% agglutination, 3⁺ indicating 75% agglutination, or 4⁺ indicating 100% agglutination.²² The endpoint of serum activity or titer is the smallest amount of serum that shows a 2⁺ agglutination.²² The strongly reactive tests can be easily seen, while a very good light source is needed to see the weak reactions.²² The tube test is much more technical and macroscopic,^{24,25} and requires 37°C incubation of the suspended antigen–antibody for up to 20 hours in a water bath.²² Results are also scored, as earlier mentioned, so are also the serial dilutions for the antibody strength.²² The tube agglutination test confirms the results and clarifies erratic or equivocal agglutination reactions of the more rapid slide agglutination test.²² The Widal test is a cheap and rapid alternative to the expensive and cumbersome blood or bone marrow culture, which may need 7 days to isolate and identify the *S. typhi*; hence, it has continued relevance in patients with febrile illness in the developing world, such as in Africa.²¹ The Widal test, however, has several limitations, including

nonspecificity,²⁶ in that there are cross-reactions with other non-Salmonella organisms such as malaria, dengue, miliary tuberculosis, endocarditis, brucellosis, and chronic liver disease, among others.²² Low sensitivity is another limitation,²⁷ but the Widal test done on convalescent-phase serum has been reported to give more reliable results with higher specificity and sensitivity.²⁷ Other studies have shown that a positive Widal test during the acute and convalescent period of typhoid fever (in sera taken 7–10 days apart) with a four-fold rise in antibody titer gives an index of suspicion.²⁸ To further compound the raging controversies on the Widal test, a study on four different brands of Widal reagents showed a lot of discrepancies; also, a fourfold rise in antibody titer was not achieved with any of the brands.²⁹ This study also found that for typhoid fever diagnosis, the use of two brands of Widal reagents in sequence could be of value, and so a single-serum sample could also be useful in a typhoid diagnosis based on an anti-“O” titer.²⁹ There is also a general consensus that the test is still valuable for the diagnosis of typhoid fever if a baseline antibody titer of the healthy afebrile individuals in the population being studied is known.²⁶ In such a study done with 200 healthy afebrile blood donors in six centers spread across southwest Nigeria, the baseline antibody titer was found to be <1:160,²⁶ while that of Turkey was found to be <1:200.²⁷ The slide agglutination test is the prevalent method for performing the Widal test in Zaria and other parts of Nigeria.³⁰

There are conflicting reports in the literature as to whether blood culture or bone marrow culture is the gold standard for diagnosing the disease correctly;^{19,31,32} it is, however, important to note that the developing nations lack the facilities to conduct these tests in most of their health care facilities. Hence, clinical acumen is relied upon most times for the diagnosis to be made before either complications or death occurs. This lack of appropriate diagnostic tools is a major problem militating against the correct management of this infection.³² The patients also do not report their symptoms early, usually reporting when complications set in, thus leading to high morbidity and mortality. A mortality rate of 22.2% was reported amongst patients treated for typhoid in a tertiary health facility in southwest Nigeria – the same area as that of this current study.³³ Furthermore, intestinal perforation was found to be the most common complication, followed by hemorrhage with septic shock.³³ Another identified problem in the sub-Saharan region is the emergence and spread of strains of *S. typhi* that are resistant to chloramphenicol, other readily available antibiotics, and recently to the quinolones.³²

These antibiotics are also used for the treatment of other infections, thereby posing serious challenges to our health care systems, placing more financial burden on patients and government, and increasing the risk of complications and death.³²

Other CD-related SD reported in this study, as shown in Tables 2 and 3, were lobar pneumonia, which accounted for 17.7%, and sepsis in many of the patients. One of the patients had hemorrhagic shock and metastatic abscesses, while another also had cerebral abscesses with raised intracranial pressure. The challenges of prompt diagnosis and treatment are late presentation of the patients in the hospital, lack of appropriate diagnostic facilities and inability of patients to afford the prescribed drugs. We are of the opinion that the patient with sepsis, hemorrhagic shock, and metastatic abscesses must have had disseminated intravascular coagulopathy as a complication of the sepsis, and this must have led to hemorrhagic shock and subsequently to death. The metastatic abscesses might also have been caused by *Staphylococcus aureus*, or any of the other organisms that are notorious for this. *S. pneumoniae* is also usually associated with lobar pneumonia in adults. A Japanese study of eleven autopsy cases of fulminant bacterial infection in adults showed that all the patients had sudden onset of hypotension and multiple organ failure culminating in unexpected death.³⁴ Blood culture in all of them confirmed bacteremia with isolation of *S. pneumoniae* (Group A, β hemolytic streptococcus) in four patients, *S. pyogenes* in another four patients, *S. dysgalactiae* subgroup equisimilis in one patient, and *Vibrio vulnificus* in another patient.³⁴ The same study further showed underlying chronic diseases in 82% of patients.³² Circulatory collapse caused by sepsis, severe pulmonary congestion, and hemorrhage accounted for death in ten (90.9%) of the eleven patients.³⁴ It is also important to note that symptoms for some days preceded SD in these patients, and the authors noted that the status of the host immune system and the virulence of the bacterium determined the onset of the fulminant bacteria infection.³⁴ There are so many factors that can be responsible for suppression of an individual's immune system in a developing nation like Nigeria, and they include chronic malnutrition, indiscriminate use of unprescribed drugs, herbal concoctions, alcoholism, substance abuse, other competing infections, HIV or acquired immunodeficiency syndrome (AIDS), and NCDs such as diabetes mellitus, cancers, and so on.

We are of the opinion that most of the patients in our current study must have had some form of fulminant bacterial infection with attendant circulatory collapse or

their infections progressed to septic shock and death from multiple organ failure. There were two patients who had unusual autopsy diagnosis as the cause of their SD. These included a 32-year-old female with severe immunosuppressive disease, which we opined was likely to have been caused by AIDS, but no test was done to confirm this at autopsy. The current prevalence of HIV/AIDS in Nigeria is 3.6%.³⁵ Mortality has continued to increase because people do not seek voluntary HIV counseling and testing (HCT), as well as treatment when needed, despite the availability of free HCT and treatment. LAUTECH is one of the recognized centers for this free HCT and HIV/AIDS treatment, but this patient never showed up for any such assistance in her lifetime. The other patient was a 60-year-old male security guard with chronic under-nutrition and features of poor personal hygiene and neglect who must have had his problem for an appreciable duration, but since there was no relative to look after his welfare, he died and was also erroneously treated as a case of SD.

This current study shows that the improvement in our public health and nutrition in Nigeria is still inadequate, and as such, chronic under-nutrition and CDs are not just causing death but they are also causing SD.

The treatment of some of these CDs responsible for SD in this study might have been covered by antimicrobials on the essential drug list in most of our primary and secondary health care facilities, where some form of free health care is being offered to citizens; in addition, there are health care services being provided by international organizations as a form of aid to developing nations like Nigeria. The Damien Foundation of Belgium provides free diagnosis and treatment for tuberculosis. The majority of the funding for the treatment of HIV/AIDS in Nigeria comes from development partners, and the main donors are the President's Emergency Plan for AIDS Relief (PEPFAR), the World Bank, and the Global Fund.³⁶

Nigeria is the largest oil producer in Africa and the 12th largest in the world,³⁷ and yet is ranked by the United Nations Development Program Human Poverty Index as 156th out of 187,³⁸ thus making it extremely difficult for the nation to cope with its numerous health challenges, amongst other challenges.

Conclusion

The developed world has moved away from the burden of CDs since the 19th century, but in Nigeria, we are still battling with CDs and malnutrition in the 21st century to the extent that these factors are even responsible for an

appreciable percentage (35.5%) of SDs in our communities. In addition to these, the chronic NCDs are also taking their toll. We must, therefore, launch a spirited public health effort to prevent both CDs and NCDs. Advocacy, health education, provision of potable water, continuous improvement in sanitation and personal hygiene, and enforcement of existing laws that ban over-the-counter sales of drugs without prescription are needed in order to prevent the emergence of antimicrobial resistance and other drug-related complications. It is also important for our government to devote greater percentages of its annual budgets to health, and tackle the issue of corruption in order to harness our resources to combat the various scourges on our health, education, and other essential areas.

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Disclosure

The authors report no conflicts of interest in this work.

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