

from about 30 per 1000 person-years in 2004 to below 20 per 1000 person-years by the second half of 2006.¹⁰

The data from Malawi and South Africa indicate that the scale-up of ART in populations with high HIV prevalence is followed by a reduction in mortality, which becomes evident at the population level after about 1 year. The rapid effect is not surprising: in the first years of a new antiretroviral programme, those accessing care are those with the most advanced disease, and the highest mortality in the absence of treatment. With continued scale-up, patients accessing care have less advanced disease,^{3,11} and the additional benefits might not be seen as rapidly at population level. These studies also illustrate some of the challenges on the road to universal access to ART: in the Karonga study, the reduction of mortality was pronounced in people living near the main road to the town, whereas an increase in mortality was noted in more remote areas.⁵ Similarly, the analyses from South Africa showed that the gains were variable across provinces, with continued increases in mortality in some provinces,⁸ and were less pronounced⁸ or absent in men.¹⁰ This finding is in line with data from IeDEA, since in South Africa (but not in Malawi) the proportion of men receiving treatment was lower than expected.¹² Continued monitoring of the public-health effect of ART at the population level, including of such inequalities,¹³ is required as the scale-up of treatment in resource-limited settings continues.

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Guidelines for anticoagulant use in acute coronary syndromes

Guidelines published by authoritative societies have important influences on clinical practice. The authors of such guidelines, who are usually experts in the topic, comprehensively review research and generally make their recommendations with an explicit grading system.

Last year the American Heart Association–American College of Cardiology (AHA–ACC) and the European Society of Cardiology each published updated

guidelines for the management of patients with acute coronary syndromes.^{1,2} The guidelines included recommendations for the use of anticoagulants in the acute management of non-ST-elevation acute coronary syndromes (NSTEMI-ACS). The committees reviewed the same research and used nearly identical criteria to rate the strength of the recommendations and to grade the quality of the evidence,^{2,3} but they interpreted the evidence for acute anticoagulant use differently, and so

reached different conclusions. Therefore, physicians who read recommendations from both the US and European societies might be confused.

The table compares the ACC–AHA and European Society of Cardiology recommendations for the use of anticoagulants in NSTEMI-ACS. The guidelines included four anticoagulants—unfractionated heparin, enoxaparin, bivalirudin, and fondaparinux—and made separate recommendations for patients managed conservatively and invasively.

There are two major areas of disagreement between the ACC–AHA and the European Society of Cardiology guidelines. The first is about the grading of the level of evidence for heparin, enoxaparin, and fondaparinux and implies that there are differences between the guideline panels in their interpretation of the criteria for the grading of evidence or their interpretation of evidence. The second area of disagreement is the class of recommendation for enoxaparin and fondaparinux. The ACC–AHA gave enoxaparin and fondaparinux a class 1 rating for conservatively and invasively managed patients, implying that there is evidence or general agreement that the treatments are useful or effective. By contrast, the European Society of Cardiology gave

enoxaparin a class 2 rating for conservatively and invasively managed patients, implying that there is conflicting evidence or divergence of opinion about the usefulness of enoxaparin, and did not recommend fondaparinux for patients undergoing urgent invasive procedures. For clinicians this is the most important area of disagreement between the guidelines because it directly affects the choice of anticoagulant; unfortunately, it is also the hardest to explain.

The differences between the two panels in the recommendations for enoxaparin are probably a result of their different interpretations of the SYNERGY trial, the meta-analysis of trials comparing enoxaparin with heparin in NSTEMI-ACS, and the OASIS-5 trial.^{4–6} The SYNERGY trial included patients with NSTEMI-ACS managed with a routine invasive strategy and found that enoxaparin was as effective as heparin but was associated with more bleeding.⁴ In all the other trials comparing enoxaparin with heparin in patients with NSTEMI-ACS, the choice of a conservative or invasive management strategy was left to the discretion of the clinician and a separate analysis of patients managed invasively in these trials remains unavailable. The results of the meta-analysis showed that enoxaparin compared with heparin reduced the number of myocardial infarctions and did not increase bleeding.⁵ The OASIS-5 trial studied conservatively and invasively managed patients with NSTEMI-ACS and found that enoxaparin was as effective as fondaparinux but caused more bleeding during the initial treatment period and was associated with excess strokes and deaths at day 30.⁶ Among the subgroup of patients managed invasively, there was an excess of catheter thrombosis with fondaparinux compared with enoxaparin and a similar excess of catheter thrombosis was seen with fondaparinux in OASIS-6.⁷

The ACC–AHA must have placed greater weight than the European Society of Cardiology on the results of the meta-analysis of randomised trials comparing enoxaparin with heparin in patients with NSTEMI-ACS and less weight on the results of individual trials (SYNERGY) and the OASIS-5 trial. By contrast, the European Society of Cardiology seemed to place greater weight on the results of the SYNERGY and OASIS-5 trials, which led them to downgrade the recommendation for enoxaparin in both conservatively and invasively managed patients. The divergent recommendations for fondaparinux

	Level	ACC/AHA 2007 guidelines ¹	ESC 2007 guidelines ²
Conservative			
Class 1	A	Heparin	Fondaparinux
		Enoxaparin	..
	B	Fondaparinux	..
	C	..	Heparin
Class 2a	B	..	Enoxaparin
Invasive			
Class 1	A	Heparin	..
		Enoxaparin	..
	B	Bivalirudin	Bivalirudin
		Fondaparinux	..
	C	..	Heparin
Class 2a	B	..	Enoxaparin

ACC=American College of Cardiology. AHA=American Heart Association. ESC=European Society of Cardiology. Class 1: evidence or general agreement that a treatment is useful or effective. Class 2: indicates that there is conflicting evidence or divergence of opinion about the usefulness or efficacy of a treatment. Class 2a: weight of evidence or opinion is in favour of usefulness or efficacy. Level of evidence reflects the quality of the evidence: Level A: data are derived from multiple randomised clinical trials or meta-analyses. Level B: data are derived from a single randomised trial or non-randomised studies. Level C: consensus opinion of experts, data derived from case studies, or standard of care.

Table: Management strategies in the 2007 AHA/ACC and the 2007 ESC Guidelines for the acute use of anticoagulants in patients with non-ST-elevation acute coronary syndromes

also reflect differences in the interpretation of the OASIS-5 trial. The excess of catheter thrombosis with fondaparinux led the European Society of Cardiology not to recommend fondaparinux in invasively managed patients. By contrast, the strong recommendation by ACC-AHA for fondaparinux in invasively managed patients implies that they did not think the risk of catheter thrombosis to be an important issue provided that a bolus dose of heparin is used at the time of the invasive procedure.

The simultaneous publication of conflicting anti-coagulation guidelines for patients with NSTEMI-ACS by organisations of such stature as the ACC-AHA and European Society of Cardiology is confusing for clinicians and has the potential to undermine the readers' confidence in the integrity of guideline development. The guideline committees did not fully explain the reasons for their choice of recommendations. The disagreements in the recommendations for enoxaparin and fondaparinux seem to stem from differences in both the interpretation of the trial data and from differences in the application of nearly identical criteria that were used by both committees to classify the evidence. Without an opportunity to review the reasoning behind each recommendation, it is difficult for readers to decide which recommendations to follow. The likelihood of disagreements could be reduced in future publications if both committees met and debated differences between their recommendations and if they included non-conflicted methodologists to ensure panellists applied criteria for evidence quality and strength of recommendations consistently. Use of a grading system that facilitates explicit consideration and interpretation of criteria might also be of benefit.⁸

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Rethinking (Product) RED

2 years ago, *The Lancet* announced the journal's partnership with (Product) RED, a business model launched by musician Bono and Bobby Shriver at the 2006 World Economic Forum. (RED) channels a portion of the profits from (RED)-branded goods to the Global Fund to Fight AIDS, Tuberculosis and Malaria. In addition to pledging US\$30 000 to (Product) RED, *The Lancet* advertised the initiative, and editorialised that "With (Product) RED they [business leaders] are...

demonstrating leadership and commitment in areas of vital societal interest".¹

In Bono's words, "(Product) RED piggybacks the excitement and energy of the commercial world to buy lifesaving AIDS drugs for Africans who cannot afford them".² Describing a recent trip to Swaziland, two (RED) ambassadors explained that "The point of our trip is to lessen the distance between (RED) shoppers around the world and the (RED) shareholders in Africa".³ But is