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Revisions to the International Health Regulations

We appreciate the attention *The Lancet* (Nov 6, p 1639)¹ has given to the process at WHO to revise the International Health Regulations (IHR). We agree that surveillance and response capacities are both essential to control public-health emergencies effectively. Your comments on pandemic influenza rightly address the need to revise the current IHR while at the same time promoting vaccine development.

The Editorial is incorrect, however, when it states, "The new IHR include no predefined lists of diseases; instead states are required to notify WHO of 'all events potentially constituting a public health emergency.'" The draft regulations, which were the subject of negotiations in Geneva on Nov 1–12, 2004,² contain a list of specific diseases for notification to WHO.

The approach taken, detailed in Annex 2 of the draft IHR, contains a list of specific diseases, including severe acute respiratory syndrome (SARS), poliomyelitis, and smallpox, which require immediate notification to WHO and a separate list of diseases that trigger the use of an algorithm. The algorithm is used to ascertain when a potential event is sufficiently serious to require notification to WHO.

Many WHO member states, including the USA, are convinced about the importance of integrating a list of diseases into the algorithm for notification to WHO of potential public-health emergencies. In fact, WHO is expected to convene an expert group to refine the proposed algorithm and integrated disease list for the next meeting of the negotiating group in February, 2005.

I declare that I have no conflict of interest.

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1 The *Lancet*. Public-health preparedness requires more than surveillance. *Lancet* 2004; **364**: 1639–40.

2 World Health Organization. Review and approval of proposed amendments to the International Health Regulations: draft revision. Geneva: WHO, 2004. http://www.who.int/gb/ghs/pdf/A_IHR_IGWG_3-en.pdf (accessed Jan 13, 2004).

GRACIA: implications for clinical practice

Francisco Fernández-Avilés and colleagues (Sept 18, p 1045)¹ randomised 500 patients with acute ST-segment elevation myocardial infarction to either a routine invasive strategy within 24 h of thrombolysis or an ischaemia-guided approach. Their primary combined endpoint of death, reinfarction, and revascularisation at 12 months arose in 21% of the ischaemia-guided group versus 9% of the invasive group (relative risk 0.44, 95% CI 0.28–0.70) and was essentially driven by the revascularisation rate. The investigators of GRACIA conclude that their finding of improved clinical outcome with a systematically invasive approach after thrombolysed myocardial infarction should affect clinical practice.

Fernández-Avilés and colleagues chose not to count in their primary endpoint the revascularisation procedures that were done during the initial hospital stay, yet from a public-payer perspective to exclude them makes no sense. All 248 patients in the invasive treatment group underwent cardiac catheterisation and 208 had revascularisation during their initial hospital stay, compared with 51 patients in the ischaemia-guided group. If these initial procedures are included in the analysis the inference is completely different, since more than twice as many combined events of death, myocardial infarction, and revascularisation then arise in the invasive compared with the ischaemia-guided group. One could stretch the authors' approach to the absurd example of an assessment of systematic prophylactic appendectomy versus symptom-guided appendectomy that concluded that the former strategy was preferable since

necessarily more emergency appendectomies were undertaken on follow-up in the latter strategy.

In their discussion, Fernández-Avilés and colleagues state that death was also reduced with the invasive strategy (6% vs 4%), yet this statement seems naive since this strategy is also compatible with a 36% increase in the relative risk of death (95% CI 0.27–1.36). The difference in the occurrence of non-fatal myocardial infarction at 1 year was also small and not significant (6% vs 4%) and could have been easily confounded by the unbalanced use of a second powerful antiplatelet agent (clopidogrel or ticlopidine). The authors did not characterise use of this class of agents that is systematically given to patients who have undergone coronary stenting (80% of the invasive group) and that is known to reduce the occurrence of myocardial infarction and unstable angina after an acute coronary syndrome.²

The findings of GRACIA do not justify the indiscriminate referral of all patients who have undergone thrombolysis for acute myocardial infarction to cardiac catheterisation and revascularisation. We believe that Fernández-Avilés and colleagues have fallen prey to an interpretative bias, and that their data show that the ischaemia-guided approach did respectably and should remain the standard of care.

We declare that we have no conflict of interest.

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1 Fernández-Avilés F, Alonso JJ, Castro-Beiras A, et al. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. *Lancet* 2004; **364**: 1045–53.

2 The Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med* 2001; **345**: 494–502.

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