



## **PARAMEDIC-2: The Adrenaline Trial**

### **Information for Emergency Department Staff**

Adrenaline has been an integral component of advanced life support from the birth of modern cardiopulmonary resuscitation (CPR) in the early 1960s. Recent prospective randomised trials<sup>1,2</sup> and observational studies<sup>3</sup> have challenged the value of using adrenaline in cardiac arrest and this view is supported by the findings of recent systematic reviews of adrenaline in out-of-hospital cardiac arrest.<sup>4,5</sup> The findings from randomised trials and observational studies indicate that giving adrenaline in out-of-hospital cardiac arrest (OHCA) increases the rate of return of spontaneous circulation (ROSC) but that longer-term outcomes (survival to hospital discharge and neurologically favourable survival) are either worse or, at best, neutral. The observational studies showing worse long-term outcome after adrenaline may be misleading if there are confounders that have not been fully adjusted for in the statistical analyses.

Although adrenaline may improve blood pressure and global blood flow to the heart and brain during CPR, animal evidence suggests that adrenaline may reduce blood flowing in the cerebral microcirculation;<sup>6</sup> thus oxygen delivery to cells may be reduced by adrenaline and neurological injury therefore made worse.

The accumulating evidence highlights the urgent need for further appropriately powered high-quality randomised controlled trials.<sup>7</sup> This need will be met by the PARAMEDIC-2 – The Adrenaline Trial, a double-blind placebo-controlled trial which will involve five ambulance service NHS Trusts (London Ambulance Service, North East Ambulance Service, South Central Ambulance Service, Welsh Ambulance Services, and West Midlands Ambulance Service) and will enrol 8000 OHCA patients.

Approval for this trial has been granted by South Central Research Ethics Committee. Given the urgency of the treatment of cardiac arrest, patients will be enrolled into the study without consent and the legal basis for this is set out in Statutory Instrument 2006 No. 2984, The Medicines for Human Use (Clinical Trials) Amendment (No. 2) Regulations 2006.



Study drug (adrenaline or placebo) will be supplied in identical packs of 10 syringes. If patients survive to be admitted to a hospital ward, the research paramedics employed for the trial will make contact with the patients (or their personal or legal representatives) and seek informed consent to participate in the follow-up of the study, which involves completing quality of life questionnaires. The outcomes that will be measured include survival to hospital admission, discharge, 30 days, 3 months, 6 months, and 12 months; and neurological status and quality of life.

**Patients enrolled in the trial and who are transported to hospital should be treated, on arrival, according to standard resuscitation procedures, including the use of adrenaline if indicated.**

Members of the public who are concerned about being enrolled in the trial will have the opportunity to opt out. The mechanism for this is likely to involve them being given a wristband that is easily identifiable by attending paramedics. Such an opt out mechanism has already been used successfully by the Resuscitation Outcomes Consortium in North America.

The Adrenaline Trial should answer once and for all the question of whether giving doses of adrenaline 1 mg during CPR improves long-term outcome from OHCA. As such, it is the most important cardiac arrest study ever to be undertaken in the United Kingdom. We anticipate that patient enrolment into the study will start in October 2014

For more information visit the trial website: [www.warwick.ac.uk/go/paramedic2](http://www.warwick.ac.uk/go/paramedic2)

## **References**

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