

fell in contrast to gains after most previous budgets.¹³ Regular, rigorous, and structured advice to governments, especially ministries of finance, given by credible experts could help to triple excise tax and raise the price of the cheapest cigarettes. Global efforts have successfully used peer interventions to change the behaviour of sex workers;¹⁴ similar peer interventions could change the behaviour of finance ministers.

Effective tobacco control over the next decade requires priority actions to increase excise taxes, while expanding coverage of plain packaging and bans on public smoking and on tobacco advertising, sponsorship, and promotion.^{1,3,5} Priority should also be given to strengthening research on tobacco use that is locally relevant—eg, by supporting the Richard Doll Centenary Classic Causes Consortium—since country-specific data can inform policy and generate vital political attention to tobacco control. Cancer Research UK will launch a global tobacco control research plan this year to generate new knowledge that can be used to support tobacco control measures. Focused actions could strengthen tobacco control worldwide and help to implement the FCTC more effectively. If so, we could bring forward the time when many tens of millions of adult smokers quit and smoking uptake among young people falls, preventing millions of premature deaths.

Prabhat Jha

Centre for Global Health Research, St Michael's Hospital and Dalla Lana School of Public Health, University of Toronto, Toronto, ONT M5B 1W8, Canada
prabhat.jha@utoronto.ca

I declare no competing interests.

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Out-of-hospital cardiac arrest: manual or mechanical CPR?

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The appropriate role for mechanical chest compression devices in pre-hospital care has been debated in recent years.¹ The quality of manual cardiopulmonary resuscitation (CPR) during out-of-hospital cardiac arrest is often less than optimum, and affects survival.² Mechanical compression devices are an attractive alternative: they never get tired, give consistent chest compressions, and allow CPR to continue during transfer of the patient. Results from two studies^{3,4} of implementation of mechanical CPR devices in the so-called real world showed higher rates of return of

spontaneous circulation and survival to discharge with mechanical CPR than with manual CPR. However, results from three randomised trials^{5–7} did not show significant survival benefit for mechanical CPR compared with manual CPR.

In *The Lancet*, Gavin Perkins and colleagues⁸ describe a pragmatic, cluster-randomised trial including adults with non-traumatic out-of-hospital cardiac arrest from four UK ambulance services. Ambulances were randomly assigned to either mechanical CPR (with the LUCAS-2 device, figure) or manual CPR. The investigators enrolled

4471 patients (1652 patients in the LUCAS-2 group, and 2819 patients in the control group). However, only 985 (60%) patients in the mechanical CPR group actually received the LUCAS-2 intervention, as did 11 (<1%) in the control group. 30 day survival (analysed by intention to treat) was similar for mechanical CPR (104 [6%] of 1652 patients) and manual CPR (193 [7%] of 2819 patients; adjusted OR 0.86, 95% CI 0.64–1.15). Neurological survival with favourable neurological outcome at 3 months was lower in the mechanical CPR group than in the manual CPR group (adjusted OR 0.72, 95% CI 0.52–0.99).

The authors should be commended for attempting a real-world clinical trial on an important issue for Emergency Medical Services (EMS) systems worldwide. This study portrays the complexities and difficulties surrounding large-scale resuscitation trials, and the importance of attention to implementation and training in the assessment of any new technology. The somewhat low device usage rate (60%) reported in this study was due to difficulties in device use (15%), unknown reasons (6%), and non-compliance (16%). Even with apparent compliance, whether operational issues resulted in implementation delays with the mechanical device is unknown. The absence of difference (or even inferiority) in outcomes in the trial group might not be due to the treatment or device itself, but to attention to training, compliance to protocols, and implementation.

When implementing a programme with a mechanical device that has weight and bulk, we cannot presume that ambulance crews would always carry the device with them when attending to a call. It would be relevant to know whether the LUCAS device was immediately started at the site or later, including in the ambulance. If later, substantial time delays in initiating mechanical CPR might have negated potential for benefit in device use.

The time from emergency call to arrival of the vehicle or ambulance crew at the patient's side, as an indicator of duration of collapse before intervention by ambulance crew, might underestimate collapse intervals. This study⁸ did not calculate collapse time or collapse duration before application of interventions. Conventional therapies for cardiac arrest seem to have minimum effect after long collapse intervals. Long intervals in the intervention group might conceal the effect of these interventions. Assessment of the effect

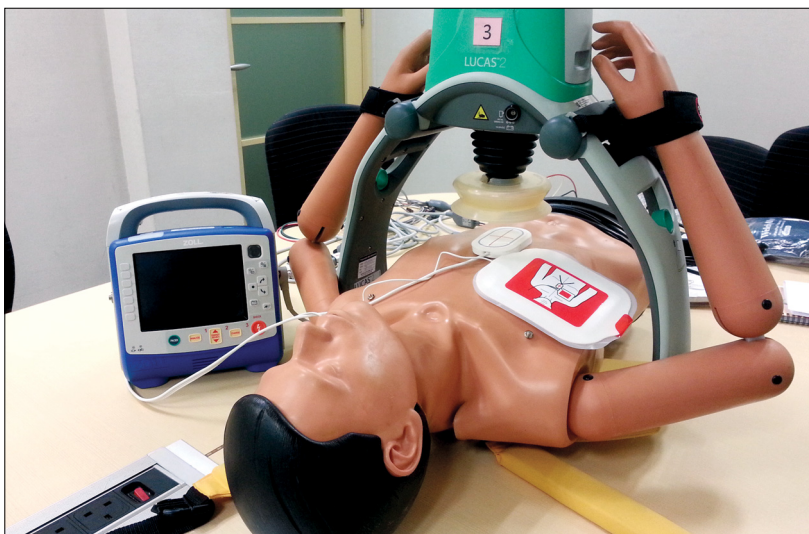


Figure: LUCAS-2 mechanical chest compression device

of this collapse interval on outcomes after mechanical CPR might throw light on the relative usefulness of this mode of resuscitation.

About 60% of cardiac arrests attended were deemed not eligible and had no resuscitation attempted (6482 of 11171). This proportion is rather high compared with that in many EMS systems internationally. This finding raises questions of selective resuscitation by ambulance crews, although the study team did monitor for enrolment bias and noted no difference between study groups.

Quality of implementation is an especially important issue with regard to the benefit or harm of mechanical CPR. Interruptions to CPR and delays in application of mechanical CPR devices are major factors that affect outcomes.⁹ Wang and colleagues showed that human error and lack of training with mechanical CPR led to prolonged intervals without chest compression.¹⁰

Attention to team training and focusing on quality of deployment of mechanical CPR devices alone can greatly improve outcomes.¹¹ The absence of quality implementation measures in this study,⁸ such as data on delays in application of the device or CPR interruptions, makes it difficult to refute the hypothesis that the outcomes noted are possibly more an effect of the quality of implementation rather than the therapy in question.

Although this study does not give us a definitive answer to the debate between manual and mechanical CPR, it does throw a spotlight on implementation

and quality. EMS services should aim to provide the best quality of CPR possible. High-quality manual CPR requires EMS commitment to training and quality review. Mechanical CPR requires the same commitment to training and attention to deployment practices. Mechanical CPR is also more costly than manual CPR. EMS systems worldwide routinely transport patients with cardiac arrest to hospital with ongoing manual CPR of doubtful quality.¹² Safety concerns for unrestrained crew using manual CPR in a moving ambulance are real. Mechanical CPR allows crews to be safely belted up and is a logical choice from the safety perspective.¹³

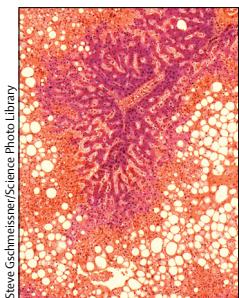
**Marcus Eng Hock Ong, Venkataraman Anantharaman*
Department of Emergency Medicine, Singapore General Hospital, 169608 Singapore (MEHO, VA); and Health Services and Systems Research, Duke-NUS Graduate Medical School, 169857 Singapore (MEHO)
marcus.ong.e.h@sgh.com.sg

MEHO is principal investigator of an industry-funded study involving a mechanical CPR device; has received grants from Laerdal Medical, grants and personal fees from Zoll Medical Corporation, and non-financial support from Bard Medical and Zoll Medical Corporation; and has a patent method of predicting patient survival licensed to Zoll Medical Corporation, and a patent system and method of determining a risk score for triage pending. VA is principal investigator in an industry-funded study on use of a mechanical CPR device in the out-of-hospital situation; has received non-financial support from Physio-Control Inc; and is a member of the Medical Advisory Board of Falck Foundation.

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Starting the battle to control non-alcoholic steatohepatitis



Non-alcoholic steatohepatitis occurs when hepatic fat, inflammation, and liver-cell injury develop in insulin-resistant individuals. Reports from US transplant registries show that non-alcoholic steatohepatitis is the third leading cause of end-stage liver disease,¹ and the second most common cause of primary liver cancer in patients listed for liver transplantation.² Yet no pharmacological therapy for non-alcoholic steatohepatitis is approved.

In *The Lancet*, Brent Neuschwander-Tetri and colleagues³ report on the effects of obeticholic acid, a synthetic farnesoid X receptor agonist, in patients with non-alcoholic steatohepatitis, in a placebo-controlled, randomised trial (FLINT). Patients were treated for 72 weeks and the primary endpoint was improvement in histology, as measured by a two-

point reduction in a composite activity histological score without worsening of fibrosis. The therapeutic phase of the trial was stopped early partly because a preplanned interim analysis showed that more patients on obeticholic acid (50 [45%] of 110) than on placebo (23 [21%] of 109) reached the primary endpoint (relative risk 1.9, 95% CI 1.3–2.8). Unexpectedly, for a trial not powered to detect fibrotic changes, the authors also reported an improvement in fibrosis: 36 (35%) of 102 obeticholic acid-treated patients regressed by one stage or more versus 19 (19%) of 98 placebo-treated patients. Neither pioglitazone, a peroxisome proliferator-activated receptor-γ agonist, nor vitamin E significantly improved fibrosis after 2 years of treatment, despite similar reductions in non-alcoholic fatty liver disease (NAFLD) activity score.⁴

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