Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

"progress is impossible without change, and those who cannot change [...] cannot change anything."[15]

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1 UK CF Trust. UK Cystic Fibrosis Registry Annual Data Report 2012, 2013. https://www.cysticfibrosis.org.uk/media/316760/Scientific%20Registry%20Review%202012.pdf (accessed Aug 5, 2014).
2 Duff AJA, Latchford GJ. Motivational interviewing for adherence problems in cystic fibrosis. *Ped Pulmonol* 2010; **45:** 211–20.
3 Arias Llorente RP, Bousoño García C, Díaz Martín JJ. Treatment compliance in children and adults with cystic fibrosis. *J Cyst Fibros* 2008; **7:** 359–67.
4 Briesacher BA, Quittner AL, Saiman L, Sacco P, Fouayzi H, Quittell LM. Adherence with tobramycin inhaled solution and health care utilization. *BMC Pulm Med* 2011; **11:** 5.
5 Eakin MN, Bilderback A, Boyle MP, et al. Longitudinal association between medication adherence and lung health in people with cystic fibrosis. *J Cyst Fibros* 2011; **10:** 258–64.
6 Sawicki GS, Tiddens H. Managing treatment complexity in cystic fibrosis: challenges and opportunities. *Pediatr Pulmonol* 2012; **47:** 523–33.
7 Golin C, Earp J, Tien H, Stewart P, Porter C, Howie L. A 2-arm, randomized, controlled trial of a motivational interviewing-based intervention to improve adherence to antiretroviral therapy (ART) among patients failing or initiating ART. *J Acq Immun Deficien Syndr* 2006; **42:** 42–51.
8 Jackson C, Eliasson L, Barber N, Weinman J. Applying COM-B to medication adherence. *Eur Health Psychol* 2014; **16:** 7–17.
9 Zolnierek KB, DiMatteo MR. Physician communication and patient adherence to treatment: a meta-analysis. *Med Care* 2009; **47:** 826–34.
10 Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999; **47:** 555–67.
11 Horne R, Weinman J, Barber N, Elliott R, Morgan M. Concordance, adherence and compliance in medicine taking. Report for the National Coordinating Centre for NHS service delivery and organisation research and development, 2005. http://www.nets.nihr.ac.uk/__data/assets/pdf_file/0009/64494/FR-08-1412-076.pdf (accessed Aug 5, 2014).
12 Bucks RS, Hawkins K, Skinner TC, et al. Adherence to treatment in adolescents with cystic fibrosis: the role of illness perceptions and treatment beliefs. *J Ped Psychol* 2009; **34:** 893–902.
13 Hibbard J, Gilburt H, The Kings Fund. Supporting people to manage their health: an introduction to patient activation, 2014. http://www.kingsfund.org.uk/sites/files/kf/field/field_publication_file/supporting-people-manage-health-patient-activation-may14.pdf (accessed July 30, 2014).
14 Brand PL, Klok T, Kaptein AA. Using communication skills to improve adherence in children with chronic disease: the adherence equation. *Paediatr Respir Rev* 2013; **14:** 219–23.
15 Shaw GB. The doctor's dilemma: preface, 1906.

ECMO as an emergency medical countermeasure

The survival benefit for patients with acute respiratory distress syndrome (ARDS) due to extracorporeal membrane oxygenation (ECMO) treatment invites consideration of whether ECMO might provide an important medical countermeasure for ARDS resulting from natural hazards or acts of terrorism. Anthrax spores, bioengineered or native avian flu strains, or chemical agents (such as chlorine gas and its derivatives) can all lead to lung injury with resulting ARDS. A framework is needed for ECMO if it is to be incorporated into our comprehensive emergency preparedness programmes.

ECMO provides continuous circulatory support or oxygenation to patients with cardiac failure and pulmonary failure. It is already established in the treatment of heart failure after cardiac surgery and has become increasingly accepted in the treatment of adults with lung injury who cannot be oxygenated by conventional means.[1]

Technological advances, facilitating the implementation of ECMO in critical care, have improved outcomes for patients with ARDS.[1] Improved technology combined with an increasing confidence in the use of ECMO from shared experiences reported at international meetings and through registries such as the Extracorporeal Life Support Organization (ELSO), has led to a substantial increase in its use (figure). Our analysis of the US Nationwide Inpatient Sample (NIS) database shows that during the past decade, ECMO support after heart surgery (post-cardiotomy) and for respiratory failure has increased by more than six times.[2] Severe acute respiratory syndrome (SARS) and H1N1 flu epidemics showed the need for lifesaving technologies and the ability of ECMO to potentially address this need in the treatment of ARDS;[1] after its successful application in these outbreaks in 2007, rates of ECMO use for respiratory failure rapidly increased.[3,4]

Portable ECMO devices are now available to allow ECMO initiation outside of a hospital setting. Some French, German, and Taiwanese centres have reported the feasibility of use of ECMO for cardiopulmonary arrest by trained interdisciplinary teams.[5,6,7] The French field ECMO programme was established to specifically deal with the anticipated need for mobile ECMO in an H1N1 epidemic.[5] This programme enhanced the possibility of incorporating ECMO into comprehensive emergency preparedness programmes as a medical


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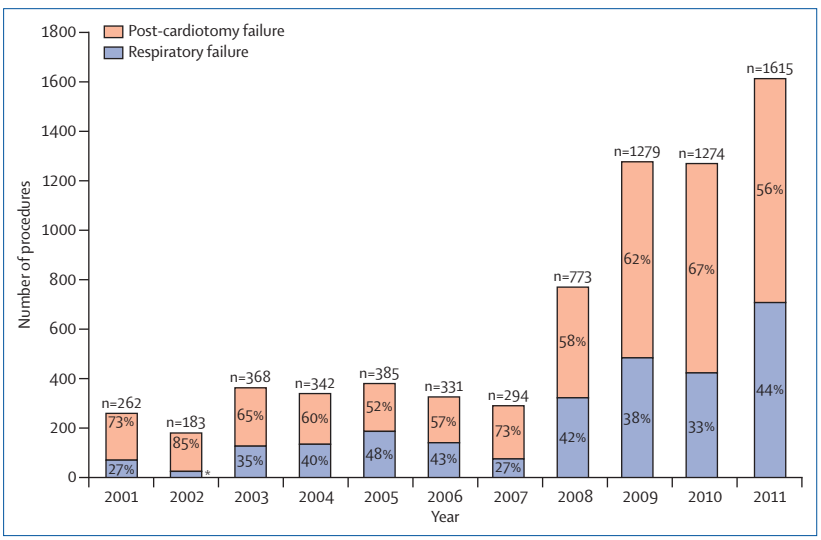

Figure: **Extracorporeal membrane oxygenation use in the USA for post-cardiotomy failure and respiratory failure, 2001–11**

*Respiratory failure is 15% in 2002. Data source: national inpatient sample data.[2]

countermeasure against epidemics or terrorist actions that could lead to ARDS. However, evidence on its use in this type of setting is limited. Although clinical information from case series, trials, and the ELSO registry provide some data, similar to other devices for disaster preparedness regimens, these devices cannot be fully tested until disaster situations arise. Bleeding, embolic, and infectious complications inherent in the use of ECMO might be increased when used in mass casualty settings in inexperienced hands. Indications for the use of ECMO could be inadvertently or erroneously expanded to include healthier patients in view of present enthusiasm for the technology because of its success in treating patients with H1N1 or SARS. Furthermore, ECMO might not be discontinued in futile cases whereby its further use leads to needless prolongation of patient discomfort and an inappropriate use of scare resources. All these factors make regulatory approval and consideration of ECMO as a medical countermeasure challenging; however, approval is needed to allow production and dissemination of sufficient devices for use in a public-health emergency.

From a regulatory perspective, the development of ECMO as a medical countermeasure needs to follow a different pathway to the usual process. It invites an even more radical change than the innovation pathway used by the US Food and Drug Administration.[8] The type and number of patients affected by acts of bioterrorism or public-health emergencies that ECMO could treat is unknown; the device cannot be fully tested until those situations occur. For present approved devices, including ECMO, the approach to their use will be based on present clinical evidence, modelling, and expert opinion. For novel devices that are potential medical countermeasures, different types and thresholds of evidence are needed to accelerate approval. Appropriate systems of assessment need to be developed that can incorporate new concepts for using accumulated data as surrogate evidence of effectiveness (and safety) in medical countermeasure settings to allow ECMOs to be included into strategies of preparedness without delays. The amount and type of evidence will vary depending on whether the device used poses high clinical risks (eg, ECMO) or low clinical risks (eg, a novel type of wound dressing).

An important consideration for regulatory bodies in approving devices for public-health emergencies is defining the indications for their use to prohibit inappropriate and futile care. An infrastructure is needed to develop decision support systems for the use of these devices by health-care professionals and to develop simulations of their use in public health emergencies. Regulatory bodies should formulate new policies to ensure effective medical care is provided and that ethical concerns of health-care professionals, patients, and families are addressed. Formal definitions of circumstances that these devices should be used in would reduce the burden on physicians in deciding when a device is appropriate or when its use is futile.

Governmental and professional agencies worldwide should collaborate to build a framework for the most appropriate use of ECMO in public-health emergencies. Such a framework would need to include the evidence needed for regulatory approval and the various clinical, ethical, and financial aspects of ECMO availability and use. Combined global experiences from implementation of ECMO in influenza epidemics, as done already in many countries, could be the first phase of such a framework. In addition to this framework, the development of new systems for data collection and plans to incorporate new technologies, such as ECMO, is imperative. Guidance on the policy debate now could lead to a measured and thoughtful use of these technologies when a disaster occurs.

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1 Peek GJ, Mugford M, Tiruvoipati R, et al. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. *Lancet* 2009; **374:** 1351–63.
2 HCUP. Overview of the National (Nationwide) Inpatient Sample (NIS). Healthcare Cost and Utilization project http://www.hcup-us.ahrq.gov/nisoverview.jsp (accessed Aug 1, 2014).
3 Brodie D, Bacchetta M. Extracorporeal membrane oxygenation for ARDS in adults. *N Engl J Med* 2011; **365:** 1905–14.
4 Davies A, Jones D, Bailey M, et al. Extracorporeal membrane oxygenation for 2009 influenza A (H1N1) acute respiratory distress syndrome. *JAMA* 2009; **302:** 1888–95.
5 Chenaitia H, Massa H, Toesca R, Michelet P, Auffray JP, Gariboldi V. Mobile cardio-respiratory support in prehospital emergency medicine. *Eur J Emerg Med* 2011; **18:** 99–101.
6 Hilker H, Philip A, Arlt M, et al. Pre-hospital cardiopulmonary resuscitation supported by ECMO—a case series of 6 patients. *Thorac Cardiovasc Surg* 2013; **61:** 45.
7 Wang CH, Chou NK, Becker LB, et al. Improved outcome of extracorporeal cardiopulmonary resuscitation for out-of-hospital cardiac arrest—a comparison with that for extracorporeal rescue for in-hospital cardiac arrest. *Resuscitation* 2014; published online June 30. DOI:10.1016/j.resuscitation.2014.06.022.
8 US FDA. Innovation pathway. US Food and Drug Administration. http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHInnovation/InnovationPathway/default.htm (accessed Aug 1, 2014).

Breaking down barriers to lung health

The Trial[1] by Kafka leaves the reader with a lasting impression of engagement with an untouchable, imposed, and bureaucratic process. The protagonist struggles to make sense of a complex machinery of forces that are beyond his control and hinder his daily life. Although these fictional trials and tribulations represent an extreme, today's respiratory and other medical researchers similarly find themselves unable to move forward with translational research because, in many instances, of rules beyond their control. This sentiment was prominent at the European Respiratory Society Presidential Summit,[2] "Breaking down barriers to lung health: a better environment for better medicines", held in Rome from July 2–3, 2014. The meeting took place under the auspices of the Italian Presidency of the Council of the European Union, which has identified respiratory diseases as a priority.[3]

By today's exigent rules, even aspirin or corticosteroids would not adhere with standards of the regulatory system. There is enormous attrition with only one approved drug from 10 000 starting molecules and the process takes around 15 years from drug discovery to regulatory approval.[4] Unsurprisingly, in respiratory medicine, there have been only nine new classes of therapy in the past 40 years.[5] Respiratory medicine has the lowest success rate of any therapeutic area in bringing new drugs to market, with 3% of drugs entering clinical trials gaining approval.[6] An overly complex regulatory environment and exaggerated concerns about safety have been powerful disincentives for people who might have otherwise become involved in drug research.

Development of a new drug costs about 1·5 billion dollars[7] and has to comply with high expectations, have a clear mechanistic proof of concept, and defined efficacy end-points. In terms of respiratory drug development, specific challenges need to be overcome, namely an incomplete understanding of pathophysiology of disease and a need for a better understanding of surrogate endpoints, making proof of concept difficult with novel innovative compounds. There is little doubt that the insistence on FEV_1 as the primary endpoint for treatments of obstructive airway disease has hampered development of new drugs because too much research has focused on this endpoint to the detriment of other potential endpoints.

An analysis of respiratory drug discovery (presented by the European Medicines Agency [EMA] at the Rome Summit) showed that during 2010–12,[8] only eight of 141 innovative medicines licensed by the EMA referred to respiratory drugs (excluding cancer and anti-infective drugs). An explanation can be found within the framework that governs clinical trials in Europe. The European Commission reported that