Shelf life considerations as EpiPen price increases

We thank Rita Rubin (Sept 24, p 1266)[1] for her explanation of EpiPen price hikes and the scrutiny facing Mylan, Canonsburg, PA, USA. Although the World Report provides excellent historical context for the controversial practice of increasing medication prices for corporate profits, we highlight shelf life designations as another issue that might contribute to increased out-of-pocket spending on EpiPens.

Expiration dates indicate a timeframe within which a medication is guaranteed safe and effective, but they are a misnomer in that medications do not necessarily become unusable after their stated shelf life—rather, pharmaceutical companies have simply not tested beyond this date.[2] Preliminary evidence[3] suggests that epinephrine might not degrade with exposure to extreme temperatures, and evidence from the US Department of Defense[4] suggests that most epinephrine administered by cartridge-needle lots in federal stockpiles were effective after their stated expiration dates. One study[5] suggests a significant difference between the bioavailability of epinephrine in outdated EpiPens as opposed to in-date devices, however, the data might be skewed because of high plasma concentrations being measured at early time points with in-date EpiPens. Controversy exists as to whether total epinephrine exposure before time of peak concentration should be used in determination of bioequivalence,[6,7] and the clinical significance has not been studied. Results from this study should also be interpreted cautiously because the sample includes a small number of injectors (n=34) with a range of post-expiration dates (1–90 months).[5]

Although pharmaceutical corporations should do more research than at present to provide customers with comprehensive shelf life information, this issue of corporate responsibility becomes particularly compelling when soaring EpiPen prices are considered. If EpiPens can be used beyond their stated shelf life of 2 years, patients, schools, hospitals, and all other affected institutions would not have to replace devices and incur steep costs so frequently.

We declare no competing interests.

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1 Rubin R. EpiPen price hike comes under scrutiny. *Lancet* 2016; **388:** 1266.
2 Diven DG, Bartenstein DW, Carroll DR. Extending shelf life just makes sense. *Mayo Clin Proc* 2015; **90:** 1471–74.
3 Parish HG, Bowser CS, Morton JR, Brown JC. A systematic review of epinephrine degradation with exposure to excessive heat or cold. *Ann Allergy Asthma Immunol* 2016; **117:** 79–87.
4 Lyon RC, Taylor JS, Porter DA, Prasanna HR, Hussain AS. Stability profiles of drug products extended beyond labeled expiration dates. *J Pharm Sci* 2006; **95:** 1549–60.
5 Simons FE, Gu X, Simons KJ. Outdated EpiPen and EpiPen Jr autoinjectors: past their prime? *J Allergy Clin Immunol* 2000; **105:** 1025–30.
6 Edwards ES, Gunn R, Simons ER, et al. Bioavailability of epinephrine from Auvi-Q compared with EpiPen. *Ann Allergy Asthma Immunol* 2013; **111:** 132–37.
7 Sclar DA. Bioequivalence evaluation of epinephrine autoinjectors with attention to rapid delivery. *Ther Clin Risk Manag* 2013; **9:** 149–51.

Open letter on the SDGs: a robust measure for universal health coverage is essential

Dear members of the Inter-Agency Expert Group on the Sustainable Development Goals (IAEG-SDGs),

We write as members of the health, academic, and research community to urge you to agree on a refinement of SDG Indicator 3.8.2, which is on financial risk protection for universal health coverage (UHC), when you meet this week at the IAEG-SDGs meeting in Geneva.

UHC has the potential to transform the lives of millions of people by bringing life-saving health care to those who need it most. Worldwide, every year 1 billion people are denied medical care because they cannot afford to pay, while 100 million are pushed into poverty by health-care costs.[1] The need for UHC couldn't be more urgent, and the inclusion of a target to achieve UHC in the SDGs is a triumph of global decision making.


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UHC means that everyone can access the quality health services they need without being pushed, or pushed further, into poverty. There are two clear indicators required to measure UHC: one for coverage (indicator 3.8.1), and one that can measure effective financial risk protection (indicator 3.8.2). We are pleased to see both aspects of UHC reflected in the framework and we congratulate you on agreeing on a robust indicator for health coverage (3.8.1).

We are, however, very concerned that indicator 3.8.2 for financial risk protection as it stands—coverage by health insurance or a public health system per 1000 population—will fail to measure the impoverishing effect of health spending meaningfully, and could undermine real progress towards UHC. Having a public health system or an insurance mechanism is, in itself, not a measure or guarantee of financial risk protection. Moreover, this indicator will not produce data that can be disaggregated by income or gender.

We endorse the WHO and World Bank-supported refinement to indicator 3.8.2: the proportion of the population with large household expenditures on health, as a total share of household expenditure or consumption. Data on household expenditure on health can be collected from existing household surveys, and this indicator allows for disaggregation, including by measures such as income and gender.

As members of the academic and research community, we want to see an indicator of financial risk protection that is scientifically robust and neutral with regard to alternative

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health financing mechanisms. A methodologically sound measure of the financial burden of health-care costs on household budgets will help academics, researchers, and health policy makers to better understand the effectiveness of different policy instruments, and can best support evidence-based policy making.

We are grateful for the opportunity to convey this message to you, and we hope that, on consideration, you will agree on an indicator for financial risk protection that supports our global ambition for quality, affordable, and equitable health-care coverage that leaves no-one behind.

We declare no competing interests.

*Di McIntyre, Martin McKee, Dina Balabanova, Chris Atim, K. Srinath Reddy, Walaiporn Patcharanarumol on behalf of 250 signatories, a full list of signatories is available in the appendix
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See Online for appendix

1 Xu K, Evans D, Carrin G, Aguilar-Rivera AM, Musgrove P, Evans T. Protecting households from catastrophic health spending. *Health Affairs* 2007; **26:** 972–983.

Genomic medicine 2025: France in the race for precision medicine

For more on **Genomic Medicine 2025 and the Aviesan Alliance** see http://www.aviesan.fr/fr/aviesan/accueil/toute-l-actualite/plan-france-medecine-genomique-2025

The French plan known as Genomic Medicine 2025 was presented this summer to Prime Minister Manuel Valls. Supported by the government and launched with a public financing of € 670 million by the year 2020, it will place France as a leader among countries involved in genomic medicine within the next 10 years. Responding to a public health challenge, this plan also encourages the emergence of a national and industrial sector for genomic medicine.

Genomic medicine is at the heart of innovation for diagnosis, prognosis, treatment, and drug administration. France must find a way to achieve this revolution, with the formidable assets of its basic, clinical and translational research.

To develop the Genomic Medicine 2025 Plan, the Aviesan Alliance brought together representatives from the research and health sectors for a year, including the Alliance for Research and Innovation in Health Industries (ARIIS), the National Health Insurance Fund (CNAM), the National Authority for Health (HAS), the Commissioner General for Investment, and the Toulouse School of Economics. Steering of the Genomic Medicine Plan will be under the responsibility of an InterMinisterial Committee and the authority of the Prime Minister. Aviesan will coordinate the monitoring of the plan and evaluate outcomes through specific indicators.

The French model of the plan involves prerogatives of medicine and science with the constant need to integrate scientific advances into health care and to facilitate access to innovation for everyone. Genomic Medicine 2025 exploits particularities of the French health-care system which integrate patient care, training, and research with the development of broad-scope actions strongly supportive of this approach (governmental plans in the fields of cancer, neurodegenerative and rare diseases, and co-definition by public and private partners of research strategies).

This plan takes into account technological progress from sequencing to the storage, analysis, and reporting of big data. Companies and academics operating in biological diagnosis, digital sector, and new sequencing technology have worked together to draw up the recommendations. The plan sets up a network of 12 sequencing services covering the whole country by 2020. A National Centre for Intensive Calculation will process the huge volumes of data generated, and provide services for health care practitioners. Standardised electronic patient medical records will be generalised.

The first ambition of Genomic Medicine 2025 is to position France among the countries leading the way in personalised medicine, with export of its expertise. The second aim is to integrate genomic medicine into the care pathway. By 2020, 235000 genomes will be sequenced each year in France, primarily for cancer and rare diseases. Beyond that, the system will be expanded to cover common diseases. A third target for 2025 is to create a national framework capable of driving scientific and technological innovation and economic growth in numerous fields including big data processing, Semantic Web and the Internet of Things, medical devices, and eHealth.

The challenge of precision medicine is also an economic one for public health policy: fewer inappropriate and extensive examinations, prescription of useless drugs or adverse reactions, gains in years of life. Last but not least, Genomic Medicine 2025 aims to be innovative in the ethical dimension. It will provide answers to the numerous questions asked by patient support groups on consent in exploitation of health data, anonymisation of data to third parties, handling of secondary discoveries and unwanted incidents.

Precise genomic medicine fosters huge hopes in people, and legitimately so, as it is changing how we define and cure disease. France is giving itself the resources needed to make this revolution a success for both patients and society as a whole.

I declare no competing interests.

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