Please note: This paper contains visible codes for electronic publishing. These will not appear in the final version and alignment of tables will be improved.

**• Please check that all queries to author [in bold type and square brackets] have been answered, including those in the references and tables. Please do not renumber the references. Any additional references can be added to the bottom of the list and unwanted references deleted from the list without renumbering. The numbering will be corrected automatically during processing**

Subscription model for antibiotic development

An unlikely answer to the global crisis in antibiotic resistance

Rebecca E Glover [Research Fellow], John Manton [Assistant Professor], Sam Willcocks [Research Fellow], Richard A Stabler [Associate Professor]

Antimicrobial Resistance Centre, London School of Hygiene and Tropical Medicine, London, UK

Correspondence to: R Stabler [Richard.Stabler@lshtm.ac.uk](mailto:Richard.Stabler@lshtm.ac.uk)

In July 2019 the National Institute for Health and Care Excellence (NICE), NHS Improvement, and NHS England announced that they will trial a “subscription model” when paying for new classes of antibiotics.1 This incentive for antibiotic research and development decouples payments to drug companies from the volume of antibiotics sold, to help encourage new products to market.

The model will use a health technology assessment process to identify a base “value” that the NHS would pay to pharmaceutical companies annually, regardless of how many prescriptions are issued. There may also be a small cost for each prescription, but the details of this new incentive have yet to be announced. The scheme’s relation to existing means of valuing antibiotics and to related strategies for infection control require scrutiny**.**

Global problem

Antibiotic resistance is recognised as a major global problem. Only one antibiotic in a new class, teixobactin, has been discovered in the past 30 years, and it was developed by a company spun out of a university research group.2 3 Policy makers will aim to protect any new antibiotic by prescribing it for only the most severely drug resistant infections, which the industry says discourages antibiotic research.

Unfortunately, even if this subscription model and other pull incentives facilitate the identification of new classes of antibiotic, resistant bacterial isolates will eventually emerge.This is the normal result of evolution given underlying mutations, drug selective pressures, and number of doses given. Teixobactin claims to be evolution proof in the laboratory,2 but these are small experiments compared with the real world experiment that occurs when antibiotics are taken on a global scale.

Although we welcome the news that the UK government will be investing in tackling antimicrobial resistance, and while the pharmaceutical sector may be a key partner in systemic approaches to managing the risk of antibiotic failure, tied investment in a particular pricing or incentive strategy poses considerable risks to public finances and policy goals.

Complex response

Revitalising the antibiotic pipeline is only one component of the complex response necessary to tackle antibiotic resistance. We must take care that innovations in pricing and incentive strategies do not sideline cheaper and potentially more effective opportunities to tackle systemic antibiotic failure. The subscription model aims to pay a fair price, but it is not clear how value will be assigned to any new antibiotics since their effectiveness in reducing antimicrobial resistance can be measured only retrospectively, after sustained use.

We should also be drawing on innovations in other treatment regimens for infectious diseases. For tuberculosis and HIV, monotherapy would be out of the question, and yet we persist in adhering to a single antibiotic course in many clinical settings.4 Investing in local surveillance may also reap dividends by allowing us to optimise and tailor current treatment options—for example, by allowing local knowledge to modify prescribing guidelines.

Perverse incentives

If the incentive is successful, patients with a multidrug resistant bacterial infection will benefit from new treatment options. From the perspective of industry, however, this fund may be most useful for already discovered compounds that are known to be effective but were never released because of economic considerations. This might result in new releases but relatively lower investment in new compounds. Creating incentives based on a societal 'value' calculation could lead to perverse incentives in the future, with companies holding back innovations in the hope that perceived value will increase as AMR rates get worse.

The dominant discourse around antimicrobial resistance draws heavily on liberal and behavioural economic models: by nudging companies to invest and urging individuals not to demand antibiotics and doctors to restrict prescription.5 6 But structural and social solutions, such as improving sick pay entitlements for workers, reducing poverty, and providing longer appointment times with better resourced primary care, can also contribute to reducing infections, antibiotic use, and antibiotic resistance in the long term.5-8 Unfortunately, these options are not a major part of the policy discourse.

This new payment model might boost drug discovery but it may also siphon away funds from known effective public health, social, and structural interventions; encourage distortions in global pharmaceutical regulatory markets; and create no long term meaningful change in the antimicrobial resistance framework. An international and interdisciplinary approach will be required if this policy is to be successful.

Understanding how this policy option came to dominate discourse is crucial. In a political context that supports market approaches in antimicrobial resistance, incentives can act as a means of capturing public resources for private gain. We must evaluate the subscription model throughout the policy cycle in order to avoid any potential risk of moving from an incentive scheme for new antibiotics towards a broader, taxpayer-funded grant for multinational pharmaceutical companies.

Competing interests: *The BMJ* has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: none**.** Further details of The BMJ policy on financial interests is here <https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-coi-form.pdf>]

Provenance and peer review: Commissioned; not externally peer reviewed.

<jrn>1 Kmietowicz Z. New antibiotics: NHS will test “pay for usefulness” model to stimulate research. *BMJ* 2019;366:l4610. [PubMed](https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=31289045&dopt=Abstract) [doi:10.1136/bmj.l4610](https://doi.org/10.1136/bmj.l4610)</jrn>

<jrn>2 Ling LL, Schneider T, Peoples AJ, et al. A new antibiotic kills pathogens without detectable resistance. *Nature* 2015;517:455-9. [PubMed](https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=25561178&dopt=Abstract) [doi:10.1038/nature14098](https://doi.org/10.1038/nature14098) </jrn>

<jrn>3 Kaeberlein T, Lewis K, Epstein SS. Isolating “uncultivable” microorganisms in pure culture in a simulated natural environment. *Science* 2002;296:1127-9. [PubMed](https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12004133&dopt=Abstract) [doi:10.1126/science.1070633](https://doi.org/10.1126/science.1070633) </jrn>

<jrn>4 Zusman O, Altunin S, Koppel F, Dishon Benattar Y, Gedik H, Paul M. Polymyxin monotherapy or in combination against carbapenem-resistant bacteria: systematic review and meta-analysis. *J Antimicrob Chemother* 2017;72:29-39. [PubMed](https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=27624572&dopt=Abstract) [doi:10.1093/jac/dkw377](https://doi.org/10.1093/jac/dkw377) </jrn>

<jrn>5 Chandler CIR. Current accounts of antimicrobial resistance: stabilisation, individualisation and antibiotics as infrastructure. *Palgrave Commun* 2019;5:53. [PubMed](https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=31157116&dopt=Abstract) [doi:10.1057/s41599-019-0263-4](https://doi.org/10.1057/s41599-019-0263-4) </jrn>

<jrn>6 Glover RE, Dangoor M, Mays N. Antibiotic resistance: don’t blame patients. *BMJ* 2019;364:l1218. [PubMed](https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=30890532&dopt=Abstract) [doi:10.1136/bmj.l1218](https://doi.org/10.1136/bmj.l1218) </jrn>

<jrn>7 Li YR, Xiao CC, Li J, et al. Association between air pollution and upper respiratory tract infection in hospital outpatients aged 0-14 years in Hefei, China: a time series study. *Public Health* 2018;156:92-100. [PubMed](https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=29408194&dopt=Abstract) [doi:10.1016/j.puhe.2017.12.006](https://doi.org/10.1016/j.puhe.2017.12.006) </jrn>

<jrn>8 Laxminarayan R, Duse A, Wattal C, et al. Antibiotic resistance-the need for global solutions. *Lancet Infect Dis* 2013;13:1057-98. [PubMed](https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=24252483&dopt=Abstract) [doi:10.1016/S1473-3099(13)70318-9](https://doi.org/10.1016/S1473-3099(13)70318-9) </jrn>