

balance between the commercial interest and patients needs. While the strategy document does speak of encouraging innovation in a range of research areas including public health, primary care, social care policy, and health systems, how are these to be secured when the strategy is so focused on industry? And what will become of drug research that is of no commercial interest to the pharmaceutical industry,⁴ such as highly successful public trials of aspirin for cardiovascular disease and magnesium sulphate for eclampsia?⁵ In the words of the House of Commons health select committee, “as the industry funds most of the research, it has a major effect on what gets researched, how it gets researched and how results are interpreted.”⁶

Furthermore, the scientific and ethical integrity of research done by clinicians and scientists and the public interest must be safeguarded. Yet the biased selection and under-reporting of industry based research and the failure to disclose relating competing interests are well documented.⁷

Lastly, it is not clear where this new strategy will leave researchers, clinicians, patients, and taxpayers. Who will own the intellectual property generated by this radical reorientation of funding for research? Above all, how far will the curiosity, rigour, and clinical

concern that have driven much medical research in the United Kingdom survive these measures?

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Antibiotics in pandemic flu

Will be essential for treating, but not preventing, bacterial pneumonia

With the continuing spread of avian H5N1 influenza a possible pandemic of human influenza becomes more likely. If a pandemic started soon no effective vaccine would be available and there would probably be a shortage of antiviral drugs. There is no evidence (yet) of the effectiveness of neuraminidase inhibitors in case of avian and pandemic influenza viruses,¹ and mortality among patients infected with H5N1 bird flu remains high, despite the use of neuraminidase inhibitors.² Resistance to antiviral drugs, which may even develop during treatment, might further limit the efficacy of these drugs.³ Given that secondary bacterial infection is an important and often fatal complication of influenza, antibiotics will also have a critical role in the event of a human pandemic.

In 1918-19, when antibiotics were not available, pandemic flu caused 20 million to 100 million deaths worldwide, with an estimated case fatality rate of between 2% and 4%. There are no data on the numbers of patients who died directly from influenza, or from secondary bacterial infections that might have been prevented with antibiotics.

How should antibiotics be used in the event of a flu pandemic? And how many patients with influenza will develop secondary bacterial pneumonia? In a largely healthy population of adolescents and adults who developed acute influenza (predominantly caused by the virus H3N2) the rate of respiratory events diagnosed by doctors and treated with prescribed anti-

biotics was around 17%, most commonly acute bronchitis and acute sinusitis. Pneumonia was diagnosed in only 1-2% of patients.^{4,5}

Can we expect a different bacterial aetiology for cases of pneumonia complicating influenza? *Staphylococcus aureus* is a common cause of post-influenza pneumonia, characterised by rapid clinical deterioration, septicaemia, and high mortality. In a comparison of pathogens isolated from patients with pneumonia during the Hong Kong influenza pandemic (1968-9) with those isolated from other patients with pneumonia during a one year period outside the epidemic, the proportion of infections caused by *Staphylococcus aureus* was more than double during the pandemic (26% v 11%), but *Streptococcus pneumoniae* was even more common (48%).⁶ Carriers of *Staphylococcus aureus*, therefore, might be particularly at risk of catastrophic complications during a flu pandemic. Whether similar rates of complications and shifts in bacterial aetiology will occur during a H5N1 pandemic is, of course, uncertain.

Should patients with mild respiratory symptoms during a pandemic be treated empirically? General practitioners will be overwhelmed with patients who

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have mild symptoms of respiratory tract infection but are concerned that they might have influenza. There is no evidence to warrant deviating from current guidelines on managing influenza, in which antibiotic treatment is usually restricted to people with signs and symptoms of pneumonia, especially the very young and very old and those with underlying diseases. Widespread prophylactic or pre-emptive use of antibiotics could encourage antibiotic resistance and thereby counterbalance any apparent short term benefits.

Although influenza may be complicated by pneumonia in only a minority of patients, in severe cases it will be difficult to distinguish purely viral pneumonia from bacterial pneumonia.⁷ Therefore, even though most patients with severe flu-like illness will have influenza, such patients must be treated with antibiotics, especially those treated in hospital.

Should current recommendations on empirical antibiotic treatment be adjusted? Patients should have antibiotics which are effective against *Staphylococcus aureus* and *Streptococcus pneumoniae*. Although all guidelines for the empirical treatment of community acquired pneumonia cover *Streptococcus pneumoniae*, *Staphylococcus aureus* poses more of a challenge. In the United States and Europe infections caused by community associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) are emerging.⁸ In some urban centres, as many as half of all *Staphylococcus aureus* samples recovered from skin and soft tissue infections among outpatients are CA-MRSA.⁹ In such places CA-MRSA should be considered the causative pathogen in episodes of severe community acquired pneumonia that need admission to hospital. Furthermore, in areas with a high prevalence of penicillin resistant *Streptococcus pneumoniae* doctors should ensure that they give β -lactam antibiotics in adequate doses.

Finally, doctors might also need to consider other measures. Pneumococcal vaccination might offer some protection against secondary bacterial infections, although randomised trials do not indicate that polysaccharide pneumococcal vaccines would be protective in preventing pneumonia and death.¹⁰ Recently introduced technology now allows rapid detection of *Staphylococcus aureus* carriage, which could be used to identify patients at increased risk for

secondary pneumonia.¹¹ Both measures would need substantial financial investments in the absence of evidence of efficacy.

Modern communication technology, rapid diagnostic testing, and better preparedness should yield real understanding of these questions in the first weeks and months of a pandemic. In the meantime we will have to rely on conventional wisdom.

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Collaborative care for depression

Is effective in older people, as the IMPACT trial shows

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Over the past decade, trials based in primary care have shown the effectiveness of collaborative care models in treating depression. Essential elements of these collaborative care programmes are the use of evidence based protocols for treatment, structured collaboration between primary care providers and mental health specialists, active monitoring of adherence to treatment and of outcomes, and (in some cases) structured programmes of psychotherapy delivered in primary care. A paper by Hunkeler and colleagues (p 259) extends the evidence for collaborative care in depression in three important

ways, finding that such care is acceptable to older patients, is effective, and has benefits that are sustained over at least two years.¹

The initial studies on collaborative care for depression showed the value of psychiatrists or psychologists working in primary care settings to improve the quality of pharmacotherapy or provide brief psychotherapy.²⁻³ Subsequent programmes attempted to improve the availability and efficiency of collaborative care through structured telephone calls with participants and nurses and bachelor-level mental health workers.⁴⁻⁵ Studies of disseminating and implementing collaborative care

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