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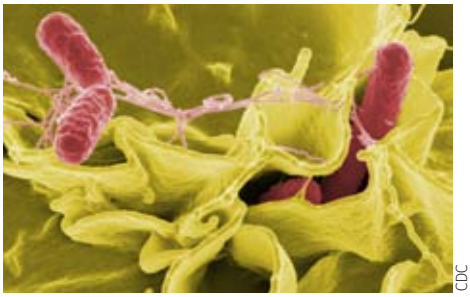
ANTIMICROBIAL RESISTANCE

New UK strategy must be set in a wider context



CDC

We welcome the editorial on the chief medical officer's intent to tackle the rise of antimicrobial resistance.[1] The remarkable success in reducing meticillin resistant *Staphylococcus aureus* bacteraemia to less than 2% exposes the rapidly growing problem of bacteraemia caused by Gram negative bacteria, particularly *Escherichia coli* (36%).[2] *E coli* differs from most agents that cause bacteraemia in that endogenous infections from gut carriage predominate.

The *E coli* population and resistance genes are dynamically connected to the wider environment and food animals.[3] This was the subject of a recent symposium,[4] which in addition to supporting the new intentions, strongly identified the international dimension of the problem of multidrug resistant *E coli* and *Klebsiella*. These organisms, which produce extended spectrum β lactamases (ESBLs), are resistant to third generation cephalosporins (such as cefotaxime), quinolones, and most antibiotics other than carbapenems. The ESBL rate in *E coli* isolated from intra-abdominal infections in 2008 was reported as 60% in India and China compared with 16.9% in the UK.[5] This large difference is probably due to the heavy and relatively uncontrolled use of antibiotics in medicine, increasingly industrialised food production systems, and water and sewage systems of variable quality in India and China. Movement of resistant *E coli*, particularly through human travel, is a growing problem, as shown by the 22.8% carriage rate of ESBL *E coli* in people in the UK of South Asian origin versus 8.1% in Europeans.[6] Strategies to control antimicrobial resistance in human and veterinary medicine must recognise that the threat from outside Europe is potentially overwhelming.

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Full response at www.bmj.com/content/346/bmj.f1601/rr/642913.

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ACCESS TO TAMIFLU TRIALS

Roche still dragging its feet

Four years after it was first promised (but not fulfilled), Roche is again offering Cochrane researchers access to its trial reports on Tamiflu. But Roche is offering less than full transparency: "In line with European Union law, each CSR [clinical study report] will be edited by Roche to ensure patient confidentiality and to protect legitimate commercial interests."[1] Furthermore, Roche says that, as a full phase III clinical study report typically consists of 2000-3000 pages, redaction will be a "large undertaking."[1]

This is smoke and mirrors. According to EU law, companies are obliged to ensure patient confidentiality in their clinical study reports. The need to edit the reports to protect commercial interests is also a red herring. In 2007, we complained to the European ombudsman when the European Medicines Agency (EMA) had refused to share clinical study reports and trial protocols with us. The ombudsman inspected the documents at the EMA and concluded that they did not contain commercially confidential information.[2] The ombudsman also noted that the documents did not identify patients by name but by identification and test centre numbers. Accordingly, nothing had been redacted in the clinical study reports on antidepressant drugs we received from the EMA. This is how it should be.

Thus, it should not be a "large undertaking" for Roche to edit its study reports because no editing is needed. Roche should hand them over to the Cochrane researchers as they are. Now. Before the patent runs out.

Big pharma often produces misleading data about drugs, and this is sometimes akin to criminal activity.[3-5] I seriously doubt that any drug company is genuinely interested in providing the transparency about its clinical trials that is needed for drugs to be used rationally, and which the EMA now provides.

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CHLORTALIDONE FOR HYPERTENSION

UK supply must be restored

In 2011 the National Institute for Health and Care Excellence (NICE) updated UK hypertension guidance.[1] Bendroflumethiazide 2.5 mg, still the most commonly prescribed UK antihypertensive,[2] was replaced by chlortalidone (12.5-50 mg) as the recommended thiazide-like diuretic, because of its much stronger evidence base. The only UK licensed preparation available is Hygroton 50 mg, which is hard to halve and unrealistic to quarter. The situation is set to worsen substantially because Hygroton is no longer reliably available in the UK. A scored 25 mg preparation of chlortalidone is available in many EU countries but is not licensed in the UK. NICE recommends indapamide as an alternative diuretic, but others have argued that there are no data from a primary prevention trial in which it has met its primary endpoint.[3] An alternative

might be bendroflumethiazide, but at a higher dose (5-10 mg).[4]

We accept NICE's evidence in favour of chlortalidone, which we believe needs to be made available in the UK. However, NICE, the Medicines and Healthcare Products Regulatory Agency (the independent regulator), and the Department of Health cannot mandate a drug's manufacture or importation. While we cannot prescribe chlortalidone for hypertension—a major risk factor for ill health[5]—UK patients and their doctors are seriously disadvantaged.

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Competing interests: None declared.

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END OF LIFE CARE

Planning for the worst together

Blackhall faces the challenges of the US system, whereby Medicare hospice benefit is payable only to those certified by a physician to be in the last six months of life and willing to forgo potentially curative treatment.[1] This places a greater emphasis on accurate prognostication, and takes away the "hope" of potentially curative treatment being offered alongside palliative care, as stipulated by the World Health Organization. The joint availability of palliative and potentially curative care allows us to work with patients to hope for the best while planning for the worst.

Patients with advanced cancer and their caregivers report difficulties in formulating and posing sensitive questions to clinicians without being prompted.[2] Conversely, clinicians often report waiting to be asked.[3] As a result, patients and carers misunderstand the illness.[4] The evidence is clear—a recent survey of 9344 people in seven European countries found that 73.9% would want to know that they had limited time to live (less than one year was the hypothetical scenario).[5] A minority (21.5%) wanted the information only if they asked. This preference should also be respected. Communication skills are key to determining the amount of information required, and patients and their families are able indicate their willingness for full or partial information if enabled to do so. As indicated in Blackhall's argument against telling patients that they are terminally ill, the true question is: how can we provide excellent care to these patients? In light of the evidence for preferences, excellent care can be determined only by asking what is wanted by those we care for, and not solely by those who provide it.

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Competing interests: None declared.

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Record access should be simpler

I have started to use the Co-ordinate My Care service.[1] Two problems are quickly apparent.

The website is too complex and difficult to navigate. It needs to have simpler aims. Ideally all the information for one patient should be on one page.

Right now you have to have an N3 connection to use it. In my area this counts out the hospice, district nurses, residential homes, and GPs on visits. The NHS commitment to protecting patient records is admirable, but it needs to become flexible enough to use. People access their bank details through the internet, so it ought to be feasible to make access to patient records secure.

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DIABETES CONTROL IN OLDER PEOPLE

Usefulness of metformin

McLaren and colleagues argue against aggressive target driven strategies for lowering glycated haemoglobin (HbA_{1c}) in older people.[1] The one exception, however, is patients with normal renal function who are taking metformin.

In these patients (as with patients treated with diet alone), there is no risk of hypoglycaemia or weight gain with lower HbA_{1c} values, or any of the concerns that apply to newer agents.[2]

Thus, metformin dose is increased gradually only to minimise gastrointestinal side effects and does not need to be adjusted according to HbA_{1c}.[3]

Indeed, full dose metformin has long been used to treat normoglycaemic women with polycystic ovary syndrome,[4] and it will probably soon be used in non-alcoholic fatty liver disease.[5]

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Limitations of targets

McLaren and colleagues claim that diabetes targets depend on the clinical situation.[1] However, funding ignores this and requires that glycated haemoglobin be below 60 mmol/mol in 75% of patients.[2]

The 25% "leeway" is soon taken up by non-adherent younger patients, so we are left with no choice other than to push everyone else below 60 mmol/mol, irrespective of any other consideration. It is probably necessary to aim for 50 mmol/mol to make sure enough patients reach the target of 60 mmol/mol.

Targets should take account of patients.

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Competing interests: Not reaching targets shows HJB up as a "bad doctor" in the Quality and Outcomes Framework.

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Cite this as: *BMJ* 2013;346:f3046