

# VIEWS & REVIEWS



## PERSONAL VIEW

### We need a drug formulary for obese people

Drugs are licensed in doses for patients of ideal weight, writes **Stephen Head**, and doctors need guidance on their effective and safe use in others

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We have an obesity epidemic, with many people weighing well above what was considered when drugs were trialled. These patients may not receive the best care possible when it comes to drug treatment.

Recommended “adult doses” of drugs need to be effective and safe for slender, shorter than average people who might weigh, say, less than 45 kg. But is a dose range that is effective and safe for a 45 kg person also effective and safe for someone three times that weight?

We often impose restrictions on specific interventions in morbidly obese patients: for example, people with a body mass index greater than 40 may be advised to lose weight before joint replacement surgery, owing to increased risk and worse outcomes. But to what extent are these increased risks and worse outcomes the result of inadequate dosing—whether in perioperative care, management of complications, or rehabilitation?

#### Uncertainty and guesswork

How should we decide the optimum drug doses for morbidly obese people? With many drugs this is uncertain, and we use guesswork. Or we simply prescribe as though the patient weighed 45 kg, because increasingly risk averse doctors are more reluctant to prescribe a dose outside the recommended range.

For some drugs we might infer a suitable dose. An example is beta blockers, where resting pulse rate is a reliable surrogate marker for adequate dosing. For other drugs, such as levothyroxine, blood test monitoring helps us to get the dose right.

Hypertension is a common problem among obese people. Titration to target is standard but can lead to dangerous polypharmacy if, at the maximum recommended dose, plasma concentrations are beneath the therapeutic threshold for effectiveness.

Suboptimal plasma concentrations may also cause therapeutic failure with antibacterials. A second drug may be tried, when the first would have worked with the right dose. If initial therapy

fails the patient might require hospital admission, at great personal and financial cost. Some antibacterials have a narrow therapeutic window that can be missed without monitoring, although this problem is less likely with some, such as beta lactams. Inappropriate prescribing also has implications for antibiotic resistance because inadequate plasma concentrations can promote the selective growth of resistant strains.<sup>1</sup>

Diabetes is common in morbidly obese people, and current dosing regimens may be insufficient. How many patients might achieve acceptable glycaemic control with metformin monotherapy if they took bigger doses than those currently licensed?

Symptomatic musculoskeletal conditions are almost inevitable in obese people. Apart from the ethical imperative to relieve symptoms, giving an insufficient dose may inadequately control symptoms and limit physical activity, promoting a vicious cycle with further weight gain or a failure to lose weight.

“Pharmacobariatrics” won’t come cheap, as new trials are needed to investigate how dosing should reflect body weight. Investment may be contentious, especially among those who regard obesity as a self induced condition for which they have little sympathy. And it might attract the drug industry, although most of the drugs that matter are off patent, with limited potential for gain in income.

The NHS and the government should support this work because it could promote health and reduce complications and costs. The costs of obesity are huge, and anything to mitigate them should be welcome.

#### Differences in pharmacodynamics

When prescribing for children we do not simply assume that they are smaller adults; similarly, obese people are not simply bigger adults. Differences in pharmacodynamics—such as absorption, distribution (lipophilic drugs may be a particular concern), metabolism (what about fatty liver?), and excretion—mean that guessing the best dose will not suffice.<sup>2,3</sup>

By using preferred treatments in effective doses treatment failures will be fewer, lessening the need for add-on or alternative treatments. These extra treatments are often newer and more expensive, with fewer long term safety data.

A huge research agenda in pharmacobariatrics would lead to better clinical practice and would benefit obese patients, the health economy, and wider society. In the United Kingdom we have a *British National Formulary* and a *British National Formulary for Children*; we also need a *British National Formulary* for obese people.

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- 1 UK Medicines Information (UKMI). Q&A 378.1: How should antibiotics be dosed in obesity? November 2013.
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