

# The 'worried-well', insulin resistance and metformin therapy

**To the Editor:** I would like to respond to the letter with the above title that appeared in a recent issue of the *Journal*.<sup>1</sup> The authors wrote: 'The decision whether to use insulin sensitisers in patients with impaired glucose tolerance is still being debated, but there is certainly no evidence that these drugs will either help the patient lose weight or prevent progression to diabetes in individuals without dysglycaemia.'

Metformin has been tried in obese individuals without diabetes as a tool for inducing weight loss. Several studies<sup>2-5</sup> found that metformin decreased body mass index (BMI), waist-to-hip ratio and total cholesterol and increased high-density lipoprotein cholesterol in obese but non-diabetic patients.

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# Zebras and bergkwaggas – the case for research on rare and very rare genetic diseases in South Africa

**To the Editor:** I recently had the privilege of learning firsthand about some very uncommon genetic diseases during a clinical infectious diseases rotation at the National Institutes of Health (NIH) in Bethesda, Maryland. Most of our patients had rare inherited immunodeficiency syndromes, such as chronic granulomatous disease and Job's syndrome, resulting in chronic intractable infections with unusual mycobacteria and fungi. These patients came from around the USA, sometimes even from other countries, for periodic elective admissions to the hospital section for a full workup. One of our patients had befriended a patient from another clinical section, and they shared a ride from Virginia when they came for their annual admissions. When I discreetly enquired what 'zebra' (the US medical student term for a very rare disease) the friend might have, the nurse replied: 'Oh that must be the guy from Tangier Island with Tangier disease.'

It turns out that Tangier disease (TD), an extremely rare (less than 50 cases reported worldwide) genetic disorder of