

CORRESPONDENCE

These letters respond to the Commentary 'The science of doping' by Donald A. Berry (*Nature* **454**, 692–693; 2008).

Doping: a paradigm shift has taken place in testing

SIR — Donald Berry claims that anti-doping tests are based on flawed statistics. Your Editorial 'A level playing field?' (*Nature* **454**, 667; 2008) goes even further in concluding that the anti-doping authorities act unscientifically. These claims neglect an abundant body of literature and ignore the paradigm shift that has taken place in anti-doping science.

Anti-doping is a forensic science, not a medical one. In medical diagnostics, biostatisticians have all the leeway to set sensitivity and specificity to an appropriate level. Such freedom is restricted in forensics: the risk of a false positive must be minimized at every step of the development, validation and application of a test. This fact alone explains why anti-doping tests do not necessarily rely on statistical reasoning, and certainly not solely on a specificity threshold, something Berry seemingly takes for granted. For the detection of exogenous testosterone in particular, anti-doping laboratories establish intervals for a reference population throughout validation processes that also include quality controls for batch acceptance. To date, no false positive has been reported among all the negative controls.

The nature of scientific evidence is also different. In forensics, the traditional assumptions of 'absolute certainty' and 'discernible uniqueness' are being progressively abandoned in favour of an empirical and probabilistic approach (see M. J. Saks and J. J. Koehler *Science* **309**, 892–895; 2005). In the fight against doping, this is embodied by the 'athlete's biological passport', an electronic

document that stores an individual's information pertaining to indirect markers of doping.

In multiplying the probabilities to estimate the specificity for the Landis case, Berry makes a basic statistical error. Indeed, successive tests are not independent in a longitudinal follow-up (P. E. Sottas *et al. Forensic Sci. Int.* **174**, 166–172; 2008).

A more thorough literature search would have prevented Berry from attempting to reinvent the wheel and from concluding that anti-doping scientists are "on the wrong path", which is presumptuous and disrespectful. The role of anti-doping science (not "doping science") is to protect clean athletes. Your Editorial may have just the opposite effect.

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Doping: probability that testing doesn't tell us anything new

SIR — In his Commentary, Donald Berry discusses Bayes' rule, noting that consideration of P , the prior probability of guilt, is essential in interpreting a positive doping result. He fails, however, to mention what the actual value of P might be in Floyd Landis's case, which I think misses an opportunity to address an important problem.

Athlete acquaintances and the news media have led me to believe that P can be very high, and in fact approach unity, in some sports. If this is true, then anti-doping measures should cease — and not because of the statistical arguments that Berry



P. DEJONG/AP

Disqualified Tour de France winner Floyd Landis still asserts his innocence.

raises, rather because the testing isn't telling us anything we don't already know.

If P is close to 1, then negative tests are most likely to be false negatives. Those who test positive might only be those who are least adept at hiding their drug use.

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Doping: ignorance of basic statistics is all too common

SIR — Donald Berry's Commentary is like a breath of fresh air in the murky world of drug testing. Unfortunately, a lack of competence in basic statistics is all too common in biology and the clinical sciences. As Berry points out, there is often a lack of accounting for pre-test

probabilities in the application of tests with known sensitivities and specificities, as well as for issues arising from multiple testing.

Even those who grasp the principles of Bayes' rule frequently make the mistake of not empirically confirming the utility of confirmatory assays. Take steroid testing, as illustrated in Berry's Figure 1 for Floyd Landis's case in 2006. Given the high sensitivity and specificity of the assay, androsterone plus 5α -androstanediol is assumed to form the basis of a conclusive set of tests for confirming positive screening results with etiocholanone plus 5β -androstanediol. In fact, the confirmatory tests can provide little additional information unless they have been shown to be independent predictors of drug positivity.

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