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► **COVER:** 'Relative drug efficacy' by Susanne Harris, inspired by the Perspective on p277.



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Gaining market access for new drugs is becoming increasingly challenging. Now, in addition to satisfying regulatory requirements for quality, safety and efficacy, a positive reimbursement decision by payers — typically based on the health benefits of the new drug relative to existing treatments, termed relative efficacy (RE) — is often needed. In their Perspective, Eichler and colleagues discuss the background to the RE debate, the methods and challenges of assessing RE, and the implications of RE for future drug development. Meanwhile, our reviews this month cover a variety of topics. Monoclonal antibodies (mAbs) are well established as a successful therapeutic modality, but carry a risk of inducing serious immune reactions as well as target-related adverse events. The safety of current mAbs and the future measures that could be taken to minimize the risk of side effects are reviewed by Hansel and colleagues. The potential of therapeutically targeting Toll-like receptors (TLRs) — using mAbs, small molecules or modified oligonucleotides — is currently receiving significant attention. O'Neill and colleagues summarize the roles of TLRs in mediating inflammation and disease, and review TLR isoform-specific agents under investigation for treating inflammatory and autoimmune diseases, viral and bacterial infections, as well as cancers. Another approach to treating various infections and cancers involves harnessing knowledge of cell-surface carbohydrate structures to develop novel vaccines. Astronomo and Burton describe specific pathogen- and tumour-associated carbohydrate targets, and discuss recent advances in addressing challenges associated with carbohydrate-based vaccine design and development. Finally, in his Perspective, Schneider considers the various issues that may be limiting the potential of virtual screening technologies to aid drug discovery programmes, and proposes possible strategies to advance the field.

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