Is it safe, is it tolerable? Why not ask the patients?

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A thought-provoking perspective by oncologist Ethan Basch, published recently in the *New England Journal of Medicine*, highlighted the absence of any patient input into establishing a drug's safety. This might seem surprising, given that distressing symptoms – which patients are best placed to report on – account for a large number of drug-related side-effects.

We know that all too often there is a disconnect between patients' and clinicians' estimates of symptom severity, with patients tending to report symptoms earlier and more frequently than physicians. By failing to collect information on patients' first-hand experience of adverse events we risk systematically underestimating a drug's safety and tolerability.

As Basch and others have argued, this issue is becoming increasingly important with greater use of targeted therapies, which are associated with mild to moderate side-effects that can persist in the long term. These types of therapy are typically reported to be 'well-tolerated' and the harmful impact of their side-effects – including treatment non-adherence – are often overlooked.

The US National Cancer Institute's CTCAE – the adverse events grading system most commonly used in cancer clinical trials – was developed in an era when cytotoxic drugs were administered intermittently and were associated with transient side-effects. There is a big difference between the tolerability of a grade 3 or 4 side-effect that lasts two days and a side-effect that may be less severe but persists in the long term. Using instruments that capture the patient experience – such as the Patient-Reported Outcomes version of the CTCAE – would help throw light on the true impact of persistent, low-grade side-effects and provide greater clarity for the development of triggers for treatment modifications.

The use of existing information technologies, such as mobile-phone-based symptom management systems, could mimimise the additional administrative burdens on clinical trials. This would also help address another limitation of the current approach to collecting data on adverse events, in that patients can report the information when they experience the problem or soon after, rather than reporting back only during clinic visits, where their recall can be subject to distortion by a variety of factors.

Collecting information directly from patients about the side-effects they are experiencing could provide valuable insight into the safety and tolerability of a particular drug and help differentiate it from other similar products.

Patients deserve a voice in defining how tolerable a drug is, and the time is right to correct an anomalous situation in which our knowledge of a drug's side-effects is based too much on second-hand impressions.

The Missing Voice of Patients in Drug-Safety Reporting, by Ethan Basch, can be accessed at http://content.nejm.org/cgi/reprint/362/10/865.pdf