

Patients and their families report difficulties in applying for such programmes, and say that they rarely receive responses. Companies that withhold a drug — because it is in short supply or not right for a patient — can find themselves on the receiving end of critical social-media campaigns highlighting individual patients. And firms worry that if a person dies or is harmed while taking a drug, it could hurt the drug's chances of being approved. No one knows how many requests parents make and how often companies approve them, but anecdotally, firms often deny drugs on the grounds that they have not been tested in children.

Proper clinical trials for childhood cancer drugs are scarce. Designing a clinical trial is never simple, but adding children to the picture complicates the process immensely. Children are not just 'small adults' — they metabolize drugs in very different ways. It is difficult to predict from adult or animal studies whether a chemotherapy drug will be more or less toxic in a child, and at what dose. The process of obtaining informed consent for children participating in a trial can also be more complicated. And companies fear that the death of a child — even if unrelated to the treatment — could bring bad publicity for a new drug.

Recent years have seen attempts to make more drugs available to treat children. In the United States, a 2003 law known as the Pediatric Research Equity Act (PREA) requires that companies develop a plan for how they will test experimental drugs in children, although many trials are exempted. A second law, called the Best Pharmaceuticals for Children Act, motivates companies to perform paediatric clinical trials by granting an extra six months of market exclusivity for the adult drug.

Overall, these laws have been successful, leading to hundreds of drug labels being updated with information for use in children. But legal loopholes often prevent children with cancer from accessing new drugs. For instance, therapies for conditions that do not affect children — such as Alzheimer's disease — are exempt from the PREA. And exemptions

intended for such diseases have been broadly applied to cancer. For example, therapies that are being trialled in adults with breast cancer are exempted because children do not get that cancer, even if the drug could treat a childhood cancer in a different organ.

Also exempted are drugs for 'orphan' diseases that affect fewer than 200,000 people in the United States. The number of orphan designations has skyrocketed in recent years — the improved ability to define the molecular basis of an individual's cancer means that diagnoses have become increasingly subdivided, and the majority of approved cancer drugs now carry this orphan designation.

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Legislation is now attempting to close those loopholes. The Research to Accelerate Cures and Equity (RACE) for Children Act, introduced to the US Congress on 14 July, would require companies to apply the PREA to any therapy with a molecular target that is relevant to both an adult and a childhood disease. It would also end the exemption for orphan diseases. Last July, the European Medicines Agency passed similar rules to make it more difficult for companies to avoid testing drugs in children. This applies when the disease has a common mechanism in adults and children, unless the drug is likely to be unsafe in children.

With Congress now out of session and focused on the upcoming US election, the RACE for Children Act is unlikely to advance before next year. But when lawmakers pick it up, they should also address problems with compassionate-use programmes — and ensure a transparent and useful process for people to gain access to unapproved drugs. They should also encourage companies to make more drugs available through market incentives, and provide increased protection should something go wrong. ■

On impact

Nature and the Nature journals are diversifying their presentation of performance indicators.

Metrics are intrinsically reductive and, as such, can be dangerous. Relying on them as a yardstick of performance, rather than as a pointer to underlying achievements and challenges, usually leads to pathological behaviour. The journal impact factor is just such a metric.

During a talk just over a decade ago, its co-creator, Eugene Garfield, compared his invention to nuclear energy. “I expected it to be used constructively while recognizing that in the wrong hands it might be abused,” he said. “It did not occur to me that ‘impact’ would one day become so controversial.”

As readers of *Nature* probably know, journal impact factors measure the average number of citations, per published article, for papers published over a two-year period. Journals do not calculate their impact factor directly — it is calculated and published by Thomson Reuters.

Publishers have long celebrated strong impact factors. It is, after all, one of the measures of their output's significance — as far as it goes.

But the impact factor is crude and also misleading. It effectively undervalues papers in disciplines that are slow-burning or have lower characteristic citation rates. Being an arithmetic mean, it gives disproportionate significance to a few very highly cited papers, and it falsely implies that papers with only a few citations are relatively unimportant.

These shortcomings are well known, but that has not prevented scientists, funders and universities from overly relying on impact factors, or publishers (*Nature's* included, in the past) from excessively promoting them. As a result, researchers use the impact factor to help

them decide which journals to submit to — to an extent that is undermining good science. The resulting pressures and disappointments are nothing but demoralizing, and in badly run labs can encourage sloppy research that, for example, fails to test assumptions thoroughly or to take all the data into account before submitting big claims.

The most pernicious aspect of this culture, as *Nature* has pointed out in the past, has been a practice of using journal impact factors as a basis for assessment of individual researchers' achievements. For example, when compiling a shortlist from several hundred job applicants, how easy it is to rule out anyone without a high-impact-factor journal in their CV.

How to militate against such a metrics-obsessed culture?

First, an approach that some have applied in the past and whose time has surely come. Applicants for any job, promotion or funding should be asked to include a short summary of what they consider their achievements to be, rather than just to list their publications. This may sound simplistic, but some who have tried it find that it properly focuses attention on the candidate rather than on journals.

Second, journals need to be more diverse in how they display their performance. Accordingly, *Nature* has updated its online journal metrics page to include an array of additional bibliometric data.

As a part of this update, for *Nature*, the *Nature* journals and *Scientific Reports*, we have calculated the two-year median — the median number of citations that articles published in 2013 and 2014 received in 2015. The median is not subject to distortion by outliers. (The two-year median is lower than the two-year impact factor: 24, down from 38, for *Nature*, for example.) For details, see go.nature.com/2arq7om.

Providing these extra metrics will not address the problem mentioned above of the diversity in citation characteristics between disciplines. Nor will it make much of a dent in impact-factor obsessions. But we hope that it will at least provide a better means of assessing our output, and put the impact factor in a better perspective.

However, whether you are assessing journals or researchers, nothing beats reading the papers and forming your own opinion. ■