had been published. Between 1987 and 2002, the proportion of relevant previous reports cited in successive reports of aprotinin trials fell from a high of 33% to only 10% among the most recent reports. Only 7 of 44 subsequent reports referenced the report of the largest trial (which was 28 times larger than the median trial size); and none of the reports referenced systematic reviews of these trials published in 1994 and 1997.

As the authors of the analysis emphasized, science is meant to be cumulative, but many scientists are not accumulating evidence scientifically. Not only are most new studies not designed in the light of systematic reviews of existing evidence but also new evidence is only very rarely reported in the context of updates of those reviews (see Chapter 8).

DISTORTED RESEARCH PRIORITIES

For most of the organizations supporting biomedical research and most of the researchers doing it, their stated aim is straightforward: to contribute information to improve people's health. But how many of the millions of biomedical research reports published every year really do make a useful contribution to this worthy cause?

Questions that are important for patients

Researchers in Bristol decided to pose a fundamental question: ‘To what extent are questions of importance to patients with osteoarthritis of the knee and the clinicians looking after them reflected in the research on this condition?’ They began by convening four focus groups – of patients, rheumatologists, physiotherapists, and general practitioners, respectively. These groups were unanimous in making clear that they did not want any more trials sponsored by pharmaceutical companies comparing yet another non-steroidal anti-inflammatory drug (the group of drugs that includes, for example, ibuprofen) against a placebo. Instead of drug trials, patients wanted rigorous evaluation of physiotherapy and surgery, and assessment of the educational and coping strategies that might help patients to manage this chronic, disabling, and often painful condition more successfully.
Of course, these forms of treatment and management offer much less scope than drugs for commercial exploitation, and so are often ignored.

How many other fields of therapeutic research would, if evaluated in this way, reveal similar mismatches between the questions about treatment effects that matter to patients and clinicians, and those that researchers are addressing? Regrettably, mismatch appears to be the rule rather than the exception.\textsuperscript{18, 19, 20, 21}

Minor changes in drug formulation rarely lead to the drugs having substantially new, more useful effects, yet these types of studies dominate research into treatments not only for arthritis but also for other chronic disorders. What a waste of resources!

Who decides what gets studied?

Clearly this situation is unsatisfactory, so how has it come about? One reason is that what gets studied by researchers is distorted by external factors.\textsuperscript{22} The pharmaceutical industry, for example, does research for its primary need – to fulfil its overriding responsibility to shareholders to make a profit. Its responsibility to patients and clinicians comes second. Businesses are driven by large markets – such as women wondering whether to use hormone replacement therapy, or people who are depressed, anxious, unhappy, or in pain. Yet only rarely in recent decades has this commercially targeted approach led to important new treatments, even for ‘mass market’ disorders. Rather, within groups of drugs, industry has usually produced many very similar compounds – so-called ‘me-too’ drugs. This is reminiscent of the days when the only bread available in supermarkets was endless variations on the white sliced loaf. Hardly surprising, then, that the pharmaceutical industry spends more on marketing than on research.

But how does industry persuade prescribers to use these new products rather than existing, less expensive alternatives? A common strategy is to commission numerous small research projects showing that the new drugs are better than giving nothing at all, while not doing any research to find out whether the new drugs are better than the existing ones. Regrettably, industry has little difficulty in finding doctors who are willing to enrol their patients in this fruitless enterprise. And the same doctors often