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Bitter Pills

They're prescribed to millions, but do the new antidepressants work? And are they worth the risk?

BY DANIEL WILLIAMS

There's really nothing funny about what happened to Rebekah Beddoe, except maybe for a little black comedy at the end. In 1999, a psychiatrist diagnosed her with postnatal depression, which she probably didn't have, and for the next three years multiple doctors treated her with drugs that she almost certainly didn't need. As episodes of deliberately cutting herself progressed to bouts of mental torment and suicide attempts, Beddoe's carers, concluding that her illness was worsening, kept upping her dosages and trying new medications. Nothing worked. Eventually, Beddoe acted on a different idea. Without telling anyone, she weaned herself off the drugs and gradually became well again. Her psychiatrist at the time assumed he was responsible for Beddoe's recovery. She remembers watching him one day from the other side of his desk, thinking that this eminent doctor was congratulating himself on having the skill to concoct precisely the right drug regimen. "I could also see his relief," Beddoe says. "It had been a difficult case, but he'd finally cracked it."

These days Beddoe, 33, spends much of her time at home in Melbourne reading up on psychiatry while working on a book about her ordeal. She's certain that what made her sick were side effects of the most commonly prescribed class of antidepressants, the selective serotonin reuptake inhibitors (SSRIs). A pharmaceutical phenomenon that began with fluoxetine (Prozac) in the late 1980s, the SSRIs rode a wave of gushing publicity to usurp the older antidepressants, the tricyclics, and reap a fortune for their makers: worldwide sales now exceed $20 billion a year. But the honeymoon is over. Even doctors who swear by SSRIs and newer variants concede that 1-2% of patients have a severe negative reaction to these drugs. That's a small percentage. But it's a small percentage of a very large number. Intractable misery is rife, it seems: in Australia last year, 12 million prescriptions for antidepressants were dispensed through the federal government's Pharmaceutical Benefits Scheme (up from 8.2 million in 1998), a figure equating to more than a million users. Do the math, says Sydney forensic psychiatrist Yolande Lucire: if only 1% of users suffer terrible side effects that aren't recognized for what they are, that's more than 10,000 Australians who've recently been disabled by a drug that was supposed to help them. "That would be enough to fill the beds in every mental hospital in the country."

Lucire's is one voice in a small but growing international chorus of SSRI skeptics. As well as highlighting side effects, these critics question whether the SSRIs do what they're supposed to do in a significant proportion of cases. Based on fresh analyses of clinical-trial results, some researchers have concluded that the drugs are scarcely more

effective than a placebo in alleviating depression. "I think they are more or less completely useless," says Dr. Joanna Moncrieff, senior lecturer in social and community psychiatry at University College London.

In an article published earlier this year in the British Medical Journal, Moncrieff and coauthor Irving Kirsch, professor of psychology at the University of Plymouth, argued that it was time for "a thorough reevaluation of current approaches to depression and further development of alternatives to drug treatment." Seldom had a piece about antidepressants so explicitly challenged the reigning orthodoxy in the mainstream medical press, and it was hailed as a breakthrough by those who oppose what they see as disease mongering by the drug industry and other groups.

The drug skeptics have had other recent victories. In the U.S. last year, the Food and Drug Administration told the drug companies to harden their warnings about the potential side effects of SSRIs. The companies' prescriber information must now feature a black-box warning - the strongest available - stating that in trials "antidepressants increased the risk of suicidal thinking and behavior" in children and adolescents with depression and other psychiatric disorders.

The fda is reviewing the results of several trials to determine whether a similar warning should be introduced for adults. British health authorities have gone further: in September, the National Health Service told doctors to stop prescribing antidepressants to under-18s in the early stages of treatment because of the link with suicidal thinking. Compared with its American and British counterparts, Australia's Therapeutic Goods Administration has taken a gentler line. Last year it reminded doctors that no antidepressant is approved in Australia for the treatment of depression in under-18s - though it knows many thousands of Australian teenagers with that diagnosis are on the drugs.

In August, a TGA bulletin acknowledged a probable link between the SSRIs and suicidal tendencies in children and adults, but overall endorsed the drugs.

Still, for perhaps the first time since the SSRIs came on the scene, those who believe the medical profession has lost its way in treating depression feel they have some momentum. "The (non-drug) approach is growing," says Dr. Jon Jureidini, head of the department of psychological medicine at the Women's and Children's Hospital in Adelaide. "I'm probably at one end of the spectrum, but there would now be plenty of psychiatrists who would be very conservative prescribers."