Evidence & Ethics: Once More into the Fray

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The last time I penned a concise argument for the Journal I focused on articles which raised interesting questions about the interplay between evidence and ethics in healthcare practice. Two articles in this month's issue highlight once more the importance of this relationship. The first is Meixel, Yanchar, and Fugh-Berman's article 'Hypoactive sexual desire disorder: inventing a disease to sell low libido' which is this month's editor's choice article. The second is Cate, van de Vathorst, Onwuteaka-Philipsen, and Agnes van der Heide's article 'End-of-life decisions for children under 1 year of age in the Netherlands: decreased frequency of administration of drugs to deliberately hasten death'.

THE 'LITTLE PINK PILL' & CREATING DISEASES?

One might be forgiven upon reading the popular press or various women's magazines for thinking that women are suffering from hitherto unseen pathological levels of low libido. Some example headlines from a variety of online publications include: 'Low Libido in Women: What's Killing Your Sex Drive?',[1] 'When Desire Dies: Bringing Your Sex Drive Back to Life',[2] 'Why Do Women Lose their Sexual Desire?',[3] and 'Sex Drive SOS: Find Out What's Behind Your Low Libido and Start Feeling Sexy Today'.[4] There is no shortage of ways suggested in these pieces for women to combat low sex drive. Practically, what has been missing until very recently, however, has been a 'little pink pill'; the so-called female Viagra.

In August this year this all changed. The Food and Drug Administration (FDA) in the United States gave its approval for a drug to treat what has been called generalised hypoactive sexual desire disorder (HSDD). Flibanserin, although approved for use in men or women, is the first drug that has been approved to treat the disorder in women.* The accompanying press release from the FDA had the following statement: 'Today's approval provides women distressed by their low sexual desire with an approved treatment option … The FDA strives to protect and advance the health of women, and we are committed to supporting the development of safe and effective treatments for female sexual dysfunction'.[5]

This news will undoubtedly be welcomed by some. The authors of this month's editor's choice article, however, are unlikely to be amongst them. In their article Meixel, Yanchar, and Fugh-Berman say that there is little evidence that HSDD is a real medical condition (***see page 859***). They argue that it was in fact created by the pharmaceutical industry in order to create a market for a drug. This is part of a range of strategies known as 'condition branding' which are sometimes employed by the pharmaceutical industry.

According to the authors, condition branding is when pharmaceutical companies adopt or invent diseases in order to develop treatments for those diseases (***see page 859***). However, in some cases the drug in question has already been developed for another condition, but is repurposed. This repurposing might happen for a number of reasons; for instance, a drug may be coming to the end of its patent for treating one condition, it may have been previously rejected by the authority responsible for licensing medicines, or it may have been found to be ineffective in treating the condition it was originally developed for. Drawing on Parry's work, the authors note three strategies which the pharmaceutical companies use in order to brand conditions and market their products, be they already existing or in development. These are (1) 'elevating the importance of an existing condition', (2) 'redefining an existing condition to reduce stigma', and (3) 'developing a new condition to build recognition for an unmet market need' (***see page 860***). It is the last of these on which they focus.

Until flibanserin was approved, all of the potential pharmacological treatments had been rejected by the Food and Drug Administration (FDA) in the United States (Meixel *et al*'s article was accepted prior to the flibanserin announcement). Yet well before attempting to gain FDA approval companies had engaged in a process of (pre-)marketing. The aim of this is to ensure that 'what industry terms a disease state is established in the minds of clinicians' (***see page 860***). Meixel and colleagues trace some of the story of how this was done in flibanserin's case and it makes worrying reading. The authors outline, in particular, how continuing medical education courses, containing spurious medical claims regarding HSDD, have been designed and used to create the condition and thus the market for a drug which can treat it. Given that flibanserin was shown to be ineffective as an antidepressant and has been denied approval previously as a treatment for HSDD (***see page 859***)—serious questions need to be asked about why it was granted approval on this occasion.

Following its second rejection there were suggestions that the FDA's decision was demonstrative of sexism and gender inequality in approaching sexual dysfunction. See, for example, a campaign called Even the Score whose site ran a petition to the FDA which stated that 'gender equality should be the standard in access to sexual dysfunction treatments'.[6] A quick web search reveals other similar petitions. It is undoubtedly the case that either temporary or permanent low libido is a problem for some women (or maybe even most women at some point in their lives). There may also be gender bias in the way society as a whole, and thus pharmaceutical companies, approach the twin issues of male and female sexual dysfunction. Nevertheless, we should be hesitant about hailing this latest development as any kind of feminist victory or thinking of the company behind the drug as a champion of women's rights. It has been argued elsewhere by Fugh-Berman and Hirsch that the sexism charge is simply a 'brilliant, misleading public relations campaign by Sprout Pharmaceuticals and its public relations firm'.[7]

In addition to the lack of evidence that low sex drive is a widespread pathological medical condition as opposed to simply a normal variation of the human condition, the evidence on the effectiveness of flibanserin also appears weak. According to the FDA press release, 'On average, treatment with Addyi increased the number of satisfying sexual events by 0.5 to one

*Although many have pointed out that "female Viagra" is a bit of a misnomer. Flibanserin works on the serotonin receptors in the brain, whereas sildenafil (Viagra) increases blood flow to the penile tissue.

additional event per month'. This is not nothing, but it is also not a great deal. Moreover, we have no information on how the drug performs in relation to non-drug therapies which could be tried to increase sex drive.

There are several pressing questions which need to be addressed here and which have a bearing on the ethics of the approval of this drug. What new evidence has been accumulated between the previous FDA rejection and this approval? Should the FDA have looked specifically at the pre-marketing and condition branding that took place? Relatedly, how ought the seemingly artificially-created pressure from interest groups have been taken into account in the approvals process? These are questions which are important not just in the case of HSDD, but all drug approvals.

EVIDENCE IN LAW AND POLICY

The utility and importance of evidence can also be seen in Cate *et al*'s article. The authors investigated the frequency of the deliberate ending of neonatal life in the Netherlands since the introduction of two measures in 2007. The first of these is routine ultrasound examinations for pregnant women at around 20 weeks. The second is making legally permissible the deliberate ending of the life of a neonate in some cases.

Cate and colleagues conducted a questionnaire amongst physicians who had reported non-sudden neonatal deaths during a 4 month period in 2010. This was compared to previous questionnaires which had been carried out pre-2007. They found that although the percentage of neonatal deaths due to withdrawing or withholding life-sustaining treatment remained relatively stable, there was a decrease in those deaths due to the explicit 'administration of drugs intended to hasten death' (***see page 795***). This is a decrease from 8% in pre-2007 years to 1% in 2010. One posited reason for this decrease is the routine 20 week ultrasound scan. The scan means that more foetuses with neural tube defects and chromosomal abnormalities are being identified and terminations of these have increased. The key decision-making point has moved to pregnancy and those who elect not to have a termination are 'less likely to ask for deliberate ending of life' once the baby is born (***see page 797***). It is also possible that the absolute numbers of babies born with such abnormalities who would require life-sustaining treatment has decreased.

While it would be useful to have a larger data sample from 2010 and other post-2007 years in order to do a more wide-ranging analysis, this data is nonetheless significant for the debate about neonatal end-of-life care. First, if there were worries that the 2007 legal provision would have increased the numbers of deliberate neonatal deaths, then this data indicates that these may have been misplaced. Second, it illustrates that laws and policies do not operate in isolation of each other. In this case the routine ultrasound scan may have negated the later need for physicians to use drugs to deliberate end neonatal lives despite this being legally permissible. Overall, however, medical practice seems to have carried on much the same as before with not much change in end-of-life decisions in general. The floodgate has not opened. There has not been an increase in the proportion of decisions to withdraw or withhold treatment generally, let alone to deliberately hasten death specifically.

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