A DEEPENING CRISIS

Triggered by aggressive marketing of prescription opioid drugs and false claims about their safety, the opioid crisis is now an epidemic that involves both prescribed and illicit drugs. Tackling it is more urgent than ever. By Liam Drew; infographic by Alisdair Macdonald.

UPWARD TRAJECTORY

In the United States, opioid prescription rates have been falling since 2011. But in the same period, the number of opioid-related deaths has increased dramatically.

MOVING UNDERGROUND

Addictions to prescription opioids have helped to create a market for heroin, an illegal opioid often adulterated with the potent opioid fentanyl.

A SAFER PRESCRIPTION

Opioid prescription rates vary markedly between countries. Some nations use this class of drug widely for pain relief without high death rates.
THE PATH TO PAIN RELIEF

Opioids can provide strong pain relief, or analgesia, but they are also extremely addictive. The benefits and risks of taking prescription and illicit opioids arise from the activation of a signalling system used by the brain to regulate numerous functions.

OPIOID RECEPTORS

There are several types of opioid receptor in cells. Prescription and illicit opioids activate the µ-opioid receptor (µOR), which inhibits the activity of neurons by two main signalling pathways.

- **Analgesia**
  The painkilling power of opioids comes, in part, from their ability to block pain signals in several locations.

- **Dependence**
  Opioid dependence results from the euphoric and rewarding effects of taking opioids, as well as from wanting to escape the effects of withdrawal. µORs in several brain regions contribute. Crucial µORs are found in the midbrain, from where they trigger the release of the neurotransmitter dopamine in the nucleus accumbens.

- **Overdose**
  µORs in the brain’s respiratory centre suppress breathing. Overactivation of these receptors through an overdose of opioids can lead to death.

The presence of µORs on the surface of many types of neuron throughout the central nervous system, as well as in the gut, mediates the diverse effects of opioids.

PAINLESS REVERSAL

Halting the opioid crisis will require action on several fronts, including these three crucial areas.

- **Alternative painkillers**
  The search for effective non-opioid painkillers continues, and new ways of targeting µORs could deliver safer opioids.

- **Decreasing dependence**
  Opioid dependency is a long-term, relapsing medical condition. The feelings of euphoria and reward that help to trigger it are caused by a spike in dopamine levels. Opioids induce this effect by halting the release of GABA, a neurotransmitter that inhibits dopamine neurons.

- **Harm reduction**
  Abruptly withdrawing prescription opioids can lead people to use illicit drugs.

  Needle-exchange services, fentanyl-contamination testing kits and naloxone (a medication that blocks the effects of opioids) can reduce disease transmission and overdose among opioid users.

Several approaches might help to tackle opioid dependency.

- **Widened treatment programmes**
  Providing a weaker opioid in combination with counselling and social support can be an effective treatment for dependency, but access to such programmes is often limited.

- **Improved monitoring**
  Better oversight of people taking prescription opioids could enable earlier intervention.

- **Fresh treatments**
  Neuroscientists are studying opioid-induced changes in neurons to develop new treatments.

In 2011, Scotland launched a programme to issue naloxone to opioid-dependent people on their release from prison. The scheme has contributed to a decrease in overdose deaths that occur in the month following release.