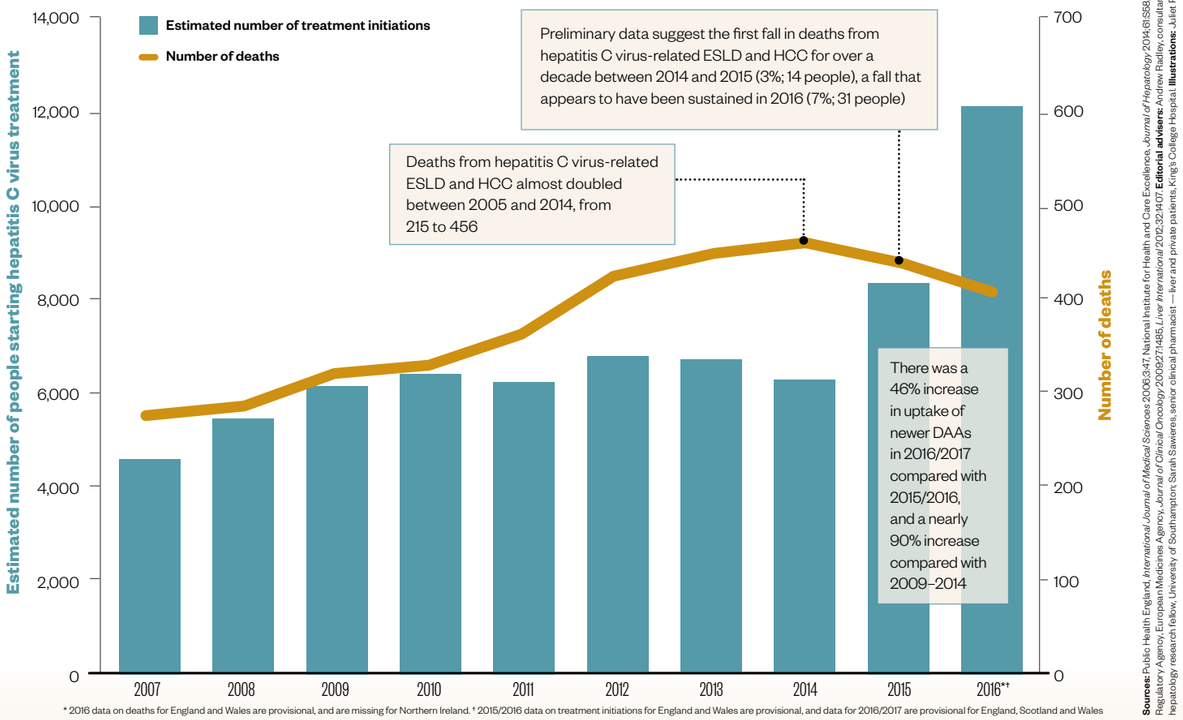
HEPATITIS C: TACKLING THE SILENT KILLER

About 200,000 people are living with hepatitis C in the UK, but it is estimated that around half of these remain undiagnosed. Identifying those at risk, offering tests and connecting those infected with treatment are crucial to tackling the disease.

BY DAWN CONNELLY

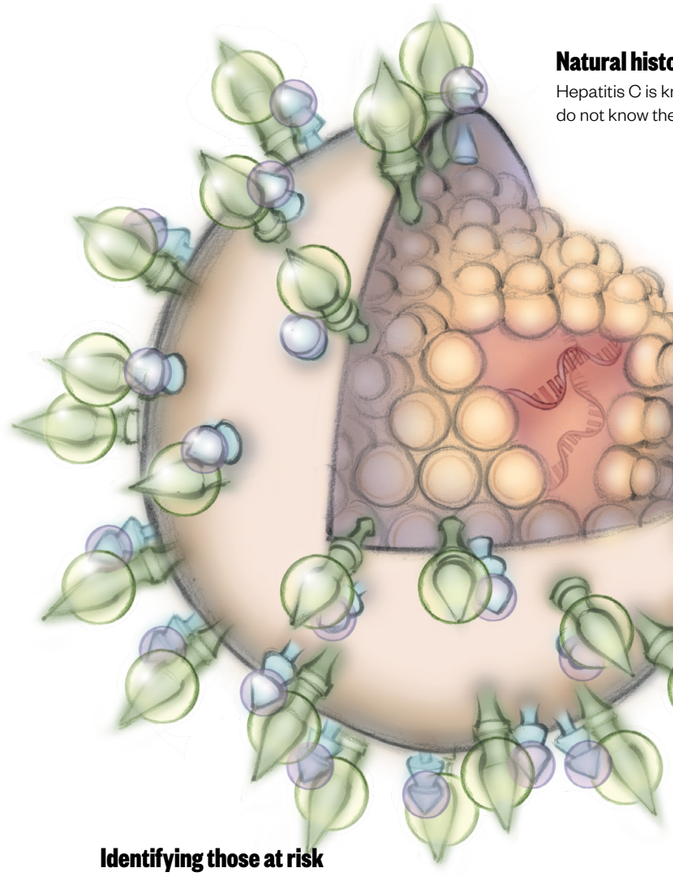
Direct-acting antivirals begin to have an impact

Following the introduction of newer, all oral, direct-acting antivirals (DAAs) in 2014, the number of patients starting treatment has increased by almost 90%, which may be responsible for the fall in end-stage liver disease (ESLD)- and hepatocellular carcinoma (HCC)-related deaths seen over the past two years.



* 2016 data on deaths for England and Wales are provisional, and are missing for Northern Ireland. † 2015/2016 data on treatment initiations for England and Wales are provisional, and data for 2016/2017 are provisional for England, Scotland and Wales

Sources: Public Health England, *International Journal of Medical Sciences* 2006;3:47; National Institute for Health and Care Excellence, *Journal of Hepatology* 2014;61:S58; Department of Health, Medicines and Healthcare products Regulatory Agency, European Medicines Agency, *Journal of Clinical Oncology* 2009;27:1485; *Liver International* 2012;32:147. **Editorial advisers:** Andrew Radley, consultant in public health pharmacy, NHS Tayside; Ryan Buchanan, hepatology research fellow, University of Southampton; Sarah Sawieres, senior clinical pharmacist — liver and private patients, King's College Hospital. **Illustrations:** Juliet Percival.



Natural history of hepatitis C

Hepatitis C is known as the "silent killer" because most people with the disease do not know they are infected until symptoms develop 20–30 years later.

Day 0: Acute infection

Mild flu-like symptoms that often go unnoticed. A minority of people may experience jaundice, dark urine, anorexia, aversion to smoking and abdominal discomfort

6 months-20 years: Chronic infection 75-85%

An estimated 15–25% of infected individuals spontaneously clear the virus

20-30 years: Cirrhosis 20-30%

Decompensated cirrhosis 3-6% per year

One-year mortality rate 20%

Hepatocellular carcinoma 1-4% per year

One-year mortality rate 53%

Death

Identifying those at risk

Hepatitis C is a blood-borne virus that is most commonly transmitted during injecting drug use, but other groups are also at risk.

People who have ever injected drugs
Injecting drug use is the main risk factor in over 90% of infected patients

Data for England (1996–2015)

People who received a blood transfusion before 1991 or blood products before 1986

People from a country with an intermediate or high prevalence of chronic hepatitis C

Babies born to mothers infected with hepatitis C

Vulnerable people including prisoners, looked-after children and young people, and homeless people

Close contacts of someone with hepatitis C, i.e. sharing razors or toothbrushes contaminated with blood

HIV-positive men who have sex with men

From discovery to cure

1989
Hepatitis C virus is identified as the cause of non-A, non-B hepatitis

1990
A hepatitis C test is developed to detect antibodies in the blood but it is not 100% reliable because it can take up to three months to develop antibodies after infection

1991
Screening of donated blood, blood products, organs and tissues for hepatitis C is introduced in the NHS

1997
The first alpha interferon, Schering-Plough's Intron A (interferon alpha-2B), is approved for treatment of hepatitis C in the UK

1999
European blood services begin screening blood with nucleic acid amplification testing (NAT), because it detects tiny hepatitis C virus RNA particles

2000
Peglyated interferon (PEGIntron; Schering Plough) is approved for treatment of hepatitis C in Europe

2001
The first combination of pegylated interferon injection and oral ribavirin is approved in Europe for treatment of all genotypes. Treatment lasts 24–48 weeks and has around a 50% cure rate in genotype 1 and 75% in genotypes 2/3

2007
The World Hepatitis Alliance is founded and launches the first world hepatitis day in July the following year

2009
The first rapid antibody test OraQuick (OraSure Technologies), which gives results in 20 minutes, receives a CE mark allowing sale in Europe

2011
The first two direct-acting antivirals (DAAs), boceprevir (Victrelis; MSD) and telaprevir (Incivek/Incivo; Vertex/Johnson & Johnson), are approved in Europe in combination with peginterferon alpha and ribavirin for genotype 1-infected patients. They improve cure rates to about 70% but worsen side effects. Treatment lasts 24–48 weeks

2014
- Second-generation DAAs sofosbuvir (Sovaldi; Gilead), simeprevir (Olysio; Janssen-Cilag), daclatasvir (Daklinza; Bristol-Myers Squibb) and ledipasvir/sofosbuvir (Harvoni; Gilead) are approved in Europe allowing interferon-free regimens for various genotypes. Treatment usually lasts 12–24 weeks, and is effective in an average of 90% of patients
- Vertex discontinues telaprevir because of competition from newer DAAs

2015
Ombitasvir/paritaprevir/ritonavir (Viekirax; AbbVie), in combination with other medicines, is approved in Europe for treatment of patients infected with genotypes 1 and 4. Dasabuvir (Exviera; AbbVie), in combination with Viekirax, is also approved for genotype 1

2016
- A combination of velpatasvir and sofosbuvir (Epclusa; Gilead), the first single treatment licensed for all genotypes, is approved in Europe, along with a combination of elbasvir and grazoprevir (Zepatier; MSD) for genotypes 1 and 4
- MSD discontinues boceprevir because of the introduction of Zepatier
- The World Health Assembly approves a global strategy to achieve elimination of hepatitis C as a public health threat by 2030. To do this, and starting from the 2015 baseline, countries and regions need to reduce new infections by 90% and reduce deaths by 65% by 2030

2017
- Combinations of sofosbuvir, velpatasvir and voxilaprevir (Vosevi; Gilead), and glecaprevir and pibrentasvir (Maviret; AbbVie) are approved in Europe for treatment of all genotypes
- Johnson & Johnson's Janssen and MSD announce they are halting development of new hepatitis C treatments because of the growing number of treatment options